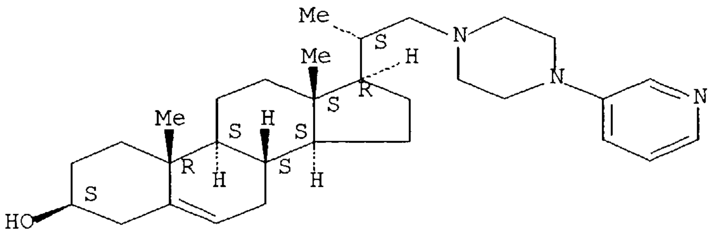
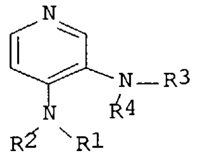
```
L23  ANSWER 1 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:291954  CAPLUS Full-text
DN   140:315075
TI   Use of MAS sterol compounds for treating diseases associated with lipid
     metabolism
IN   Grondahl, Christian; Lindenthal, Bernhard
PA   Novo Nordisk A/S, Den.; Schering AG
SO   PCT Int. Appl., 34 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
PI   WO 2004028544    A1    20040408      WO 2003-DK619    20030923
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE,
             GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
             LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
             OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
             TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
PRAI DK 2002-1417      A    20020925
OS   MARPAT 140:315075
AB    Certain sterols can be used for increasing the HDL cholesterol to non-
      HDL cholesterol ratio, for treatment and/or prevention of
      atherosclerosis, for treatment and/or prevention of hyperlipidemia, for
      treatment of diabetic dyslipididemia, for treatment of
      hypercholesterolemia, for treatment of diseases of illness related to
      metabolic dysfunction, for treatment of obesity or obesitas related
      diseases, and for the treatment of neurol. diseases.
IT   677309-74-9
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
(MAS sterol compds. for treating diseases associated with lipid metabolism)
RN   677309-74-9  CAPLUS
CN   Pregn-5-en-3-ol, 20-methyl-21-[4-(3-pyridinyl)-1-piperazinyl]-,
     (3β,20S)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
```



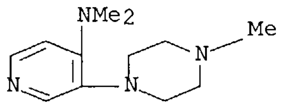
```
RE.CNT  5      THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 2 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:268215  CAPLUS Full-text
DN   140:287859
TI   New catalysts for the dimerization of aliphatic polyisocyanates.
IN   Koecher, Juergen; Laas, Hans-Josef
PA   Bayer A.-G., Germany
SO   Ger. Offen., 9 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.       KIND  DATE          APPLICATION NO.  DATE
     ---------------  ----  --------      ---------------  --------
PI   DE 10244216       A1   20040401      DE 2002-10244216 20020923
PRAI DE 2002-10244216       20020923
OS   MARPAT 140:287859
GI
```



I

```
AB    3,4-Bis(dialkylamino)pyridines I (R1, R2 = C1-6 alkyl or R1R2 = N-
      containing C5- or C6 ring system, including pyrrolidine-, piperidine-,
      piperazine- or morpholine-ring, R3, R4 = R1, R2 ) (catalysts for
      isocyanurate-free dimerization of aliphatic diisocyanates to uretdione
      polyisocyanates) are prepared by reacting of 3-bromo-4-
      dialkylaminopyridine with secondary aliphatic amines and bases in the
      presence Pd complexes and P-containing ligands. Reacting 22.0 g 3-bromo-
      4-dimethylaminopyridine with 15.0 g of Na tert-butylate and 11.1 mL of
      pyrrolidine in the presence of 2.0 g of
      tris(dibenzylidenacetone)dipalladium(0) and 2.75 g of racemic 2,2'-
      bis(diphenylphosphino)-1,1'-binaphthyl in toluene for 7 h at 70° gives
      13.7 g of 3-pyrrolidino-4-dimethylaminopyridine.
IT   676144-92-6P
     RL: CAT (Catalyst use); IMF (Industrial manufacture); PREP
(Preparation);
     USES (Uses)
        (3,4-Bis(dialkylamino)pyridines, manufacture from 3-bromo-4-
        dialkylaminopyridine and secondary aliphatic amines as catalysts for
        dimerization of aliphatic polyisocyanates)
RN   676144-92-6  CAPLUS
CN   4-Pyridinamine, N,N-dimethyl-3-(4-methyl-1-piperazinyl)- (9CI)  (CA
     INDEX NAME)
```



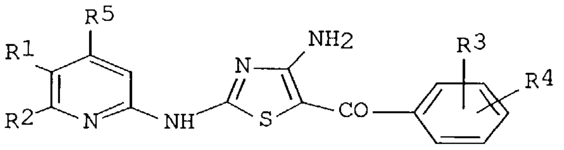
L23 ANSWER 3 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:143146 CAPLUS Full-text
DN 140:181441
TI Preparation of antiproliferative 2-(pyridylamino)thiazole compounds
IN Chong, Wesley Kwan Mung; Duvadie, Rohit Kumar; Li, Lin; Yang, Yi
PA Pfizer Inc., USA
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004014904	A1	20040219	WO 2003-IB3181	20030729

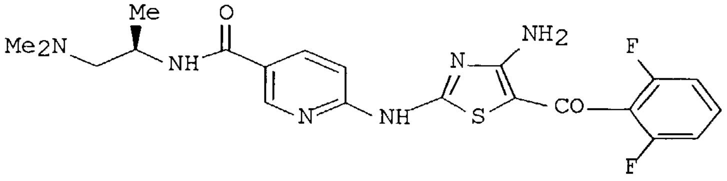
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI US 2002-402408P P 20020809
OS MARPAT 140:181441
GI



I



II

AB Thiazole derivs. of formula I [R1 = H, alkenyl, alkylamino, aryl, heteroaryl, cycloalkyl, etc.; R2, R5 = H, halo, alkyl, OMe, OH, amino, SH, SMe, etc.; R3, R4 = H, halo, OMe, alkyl] are prepared The compds. and pharmaceutical compns. containing them may be used in inhibiting and/or modulating protein kinases, in treating or preventing diseases associated with protein kinases, and/or in treating or preventing cellular proliferative diseases. Thus, II was prepared, and had IC50 and IC90 of 0.0026 and 0.0057 μM resp. against HCT-116 cells.

IT **571189-49-6P 657410-79-2P 657410-80-5P**

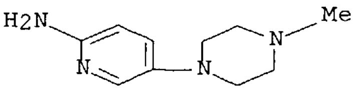
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(preparation of antiproliferative (pyridylamino)thiazole compds.)

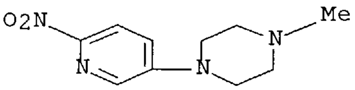
RN 571189-49-6 CAPLUS

CN 2-Pyridinamine, 5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



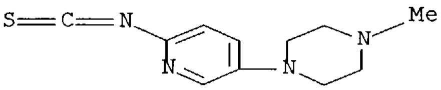
RN 657410-79-2 CAPLUS

CN Piperazine, 1-methyl-4-(6-nitro-3-pyridinyl)- (9CI) (CA INDEX NAME)



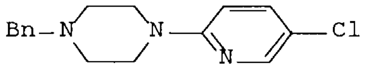
RN 657410-80-5 CAPLUS

CN Piperazine, 1-(6-isothiocyanato-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

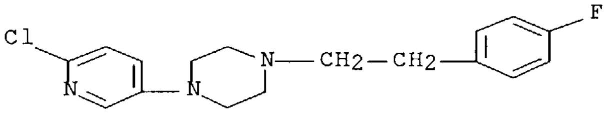
L23 ANSWER 4 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:137915 CAPLUS Full-text
DN 140:357297
TI A short and efficient synthesis of N-aryl- and N-heteroaryl-N'-(arylalkyl)piperazines
AU Michalik, Dirk; Kumar, Kamal; Zapf, Alexander; Tillack, Annegret; Arlt, Michael; Heinrich, Timo; Beller, Matthias
CS Leibniz-Institut fur Organische Katalyse (IfOK), Universitat Rostock e.V., Rostock, D-18055, Germany
SO Tetrahedron Letters (2004), 45(10), 2057-2061
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier Science B.V.
DT Journal
LA English
GI



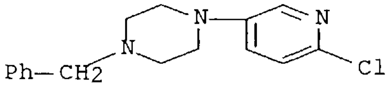
I

AB A synthesis of N-aryl- and N-heteroaryl-N'-(aralkyl)piperazines, e.g., I, using palladium-catalyzed amination of aryl bromides and heteroaryl chlorides with N-benzyl- or N-(arylethyl)piperazines, is reported. The coupling reaction proceeded in high yield and good selectivity using either diadamantyl-n-butylphosphine, 2-(dicyclohexylphosphino)-2'-(N,N-dimethylamino)biphenyl, or 2-(di-tert-butylphosphino)biphenyl as ligand. Applying an automated parallel synthesizer the preparation of a small library of potentially bioactive compds. is easily achieved.

IT **681468-64-4P**
RL: BYP (Byproduct); PREP (Preparation)
(byproduct from the regioselective preparation of N-(chloropyridinyl)-N'-fluorophenethylpiperazine via hydroamination of fluorostyrene with benzylpiperazine followed by debenzylation and arylation with dichloropyridine)
RN 681468-64-4 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)-4-[2-(4-fluorophenyl)ethyl]- (9CI) (CA INDEX NAME)



IT **633283-62-2P**
RL: BYP (Byproduct); PREP (Preparation)
(regioisomeric byproduct from the regioselective preparation of N-benzyl-N'-(chloropyridinyl)piperazine via arylation of N-benzylpiperazine with dichloropyridine)
RN 633283-62-2 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

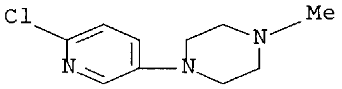


RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

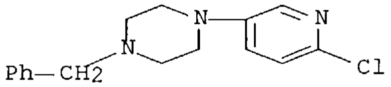
L23 ANSWER 5 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:861302 CAPLUS Full-text
DN 140:27744
TI Selective Amination of Polyhalopyridines Catalyzed by a Palladium-Xantphos Complex
AU Ji, Jianguo; Li, Tao; Bunnelle, William H.
CS Neuroscience Research Global Pharmaceutical Research and Development, Department-R47W AP9A-1, Abbott Laboratories, Abbott Park, IL, 60064, USA
SO Organic Letters (2003), 5(24), 4611-4614
CODEN: ORLEF7; ISSN: 1523-7060
PB American Chemical Society
DT Journal
LA English

AB Amination of 5-bromo-2-chloropyridine catalyzed by a palladium-xantphos complex predominately gives 5-amino-2-chloropyridine product in 96% isolated yield and excellent chemoselectivity. Amination of 2,5-dibromopyridine under the same conditions exclusively affords 2-amino-5-bromopyridine.

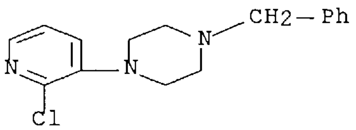
IT **633283-61-1P 633283-62-2P 633283-64-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of pyridine derivs. via chemoselective amination of polyhalopyridines using a palladium-xantphos complex as a catalyst)
RN 633283-61-1 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 633283-62-2 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)

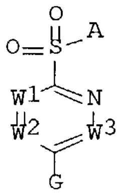


RN 633283-64-4 CAPLUS
CN Piperazine, 1-(2-chloro-3-pyridinyl)-4-(phenylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

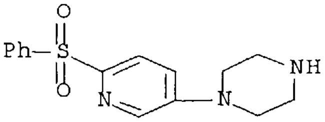
```
L23  ANSWER 6 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:696870  CAPLUS Full-text
DN   139:230794
TI   Preparation of pyridyl phenyl sulfones as 5-HT6 receptor modulators
IN   Tenbrink, Ruth E.; Kortum, Steven W.
PA   Pharmacia & Upjohn Company, USA
SO   PCT Int. Appl., 48 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   WO 2003072548      A1   20030904      WO 2003-US5263    20030220
     WO 2003072548      C1   20031224
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
            CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
            GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
            LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
            PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
            UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD,
            RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
            CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
            NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
            ML, MR, NE, SN, TD, TG
     US 2003186968      A1   20031002      US 2003-371391    20030220
PRAI US 2002-359174P    P    20020222
OS   MARPAT 139:230794
GI
```



I

```
AB   The title compds. [I; W1-W3 = N, CR (provided that no more than one of
     W1-W3 are N, and further provided that when W2 = N that W3 is not
     C(CN)); A = 5-6 membered monocyclic aromatic ring, 8-10 membered fused
     aromatic ring, etc.; G = (un)substituted piperazino, 1,4-diazepan-1-yl,
     pyrrolidino, piperidino, etc.], useful for treating a disease or
     condition in a mammal wherein a 5-HT receptor, such as a 5-HT6 receptor,
     is implicated and modulation of a 5-HT function is desired, were
     prepared  Thus, reacting 5-chloro-2-pyridinyl Ph sulfone (preparation
     given) with piperazine in MeCN afforded I [W1-W3 = CH; A = Ph; G =
     piperazino].  All of the exemplified compds. I are 5-HT ligands, with
     the ability to displace >50% of a radiolabeled test ligand from one or
     more 5-HT receptor subtypes at 1 μM.  Pharmaceutical composition
     comprising the title compound I was claimed. Use of the isotopically
     labeled compds. I in performing positron emission tomog., NMR imaging
     and single-photon-emission computed tomog. was claimed.
IT   594847-72-0P
     RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
```

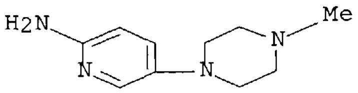
(Uses)(preparation of pyridyl Ph sulfones as 5-HT6 receptor modulators)
RN 594847-72-0 CAPLUS
CN Piperazine, 1-[6-(phenylsulfonyl)-3-pyridinyl]- (9CI) (CA INDEX NAME)



RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

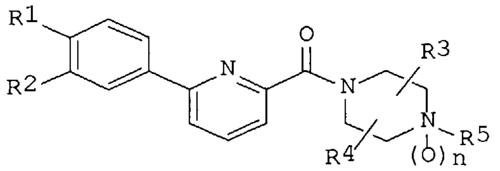
```
L23  ANSWER 7 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:591180  CAPLUS Full-text
DN   139:149646
TI   Preparation of pyrido[2,3-d]pyrimidin-7-ones as cdk4 inhibitors
IN   Barvian, Mark Robert; Booth, Richard John; Quin, John, III; Repine,
     Joseph Thomas; Sheehan, Derek James; Toogood, Peter Laurence; Vanderwel,
     Scott Norman; Zhou, Hairong
PA   Warner-Lambert Company Llc, USA
SO   PCT Int. Appl., 146 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2003062236      A1   20030731      WO 2003-IB59     20030110
     WO 2003062236      C1   20031224
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
             TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,
             ML, MR, NE, SN, TD, TG
     US 2003149001      A1   20030807      US 2003-345778   20030116
PRAI US 2002-350877P    P    20020122
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

AB    Title compds. I [wherein X1, X2, X3 = independently H, halo, alkyl,
      (un)substituted amino, acyl, carbamoyl, sulfamoyl, etc.; R1 =
      independently H, halo, alkyl, haloalkyl, hydroxyalkyl, cycloalkyl; R2,
      R4 = independently H, halo, (un)substituted alkyl, amino, acyl,
      sulfamoyl, carbamoyl, etc.; R3 = H, aryl, alkyl, alkoxy, cycloalkyl,
      heterocyclyl; R1CCR2 = 3-7 carbocyclic or heterocyclic ring; and their
      pharmaceutically acceptable salts, esters, amides, or prodrugs] were
      prepared as cyclin-dependent kinases 4 (cdk4) inhibitors.  Examples
      include 135 invention compds., three biol. assays, one tablet
      formulation, and a parenteral solution  For example, compound II·2.2HCl
      was prepared by the solventless reaction of 6-bromo-8-cyclopentyl-2-
      methylsulfinyl-8H- pyrido[2,3-d]pyrimidin-7-one with 4-(6-aminopyridin-
      3-yl)piperazine-1- carboxylic acid tert-Bu ester at 1200C for 1 h,
      followed by deprotection in the presence of gaseous HCl.  II selectively
      inhibited cdk4 over cdk2 with IC50 values of 0.016 μM and 6.052 μM,
      resp.  Thus, I and their formulations are useful for treating cell
      proliferative disorders, such as cancer, atherosclerosis, and restenosis
      (no data).
IT    571189-49-6, 5-(4-Methylpiperazin-1-yl)pyridin-2-ylamine
      RL: RCT (Reactant); RACT (Reactant or reagent)
      (preparation of pyrido[2,3-d]pyrimidinones as cdk4 inhibitors for
      treating cell proliferative disorders)
RN    571189-49-6  CAPLUS
```

CN 2-Pyridinamine, 5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

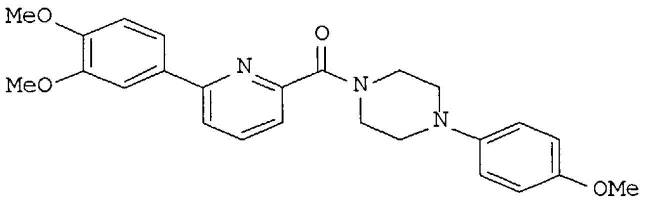


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 8 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:977792  CAPLUS Full-text
DN   138:55982
TI   Preparation of 1-(6-phenylpyridine-2-carbonyl)piperazine derivatives as
     phosphodiesterase (PDE) IV inhibitors
IN   Iwata, Masahiro; Kawano, Noriyuki; Kaizawa, Hiroyuki; Takuwa, Tomofumi;
     Tsukamoto, Issei; Seo, Ryushi; Yahiro, Kiyoshi; Kobayashi, Miki;
Takeuchi,
     Makoto
PA   Yamanouchi Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 58 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2002102778      A1   20021227      WO 2002-JP5926   20020613
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     JP 2003064057      A2   20030305      JP 2002-172377   20020613
     EP 1396487         A1   20040310      EP 2002-738703   20020613
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
PRAI JP 2001-182296     A    20010615
     WO 2002-JP5926     W    20020613
OS   MARPAT 138:55982
GI
```



I



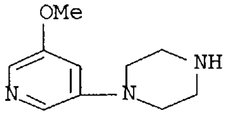
II

AB   The title compds. I [wherein R1 and R2 = independently H, halo, alkyl, (un)substituted alkyloxy, amino, alkylamino(alkoxy), dialkylamino(alkoxy), NHCO-alkyl, O-alkylene-CO2R0, or (hetero)cyclylalkoxy; or R1 and R2 together form a ring; R0 = H, alkyl, or (un)substituted PhCH2; R3 and R4 = independently H, (un)substituted alkyl, halo, CO2R0, CONH2, CONR0-alkyl, (un)substituted (hetero)cyclyl(carbonyl), alkyl-CO, or CN; or R3 and R4 together are alkylene or oxo; R5 = H, alkyl, (alkylene)CO2R0, CONH2, CONR0-alkyl, alkyl-CO, (un)substituted (hetero)cyclyl(hydrocarbonyl), (hetero)cyclyl(alkylenyl)(carbonyl), CO2-alkylene-(hetero)cyclyl, or carbamoyl, etc.; n = 0-1; with provisos] and pharmaceutically acceptable salts thereof are prepared as PDE IV inhibitors. I are useful for the prevention and treatment of respiratory tract diseases, asthma, and chronic obstructive pulmonary diseases (COPD) (no data). For example, a THF solution of 6-(3,4-dimethoxyphenyl)pyridine-2-carboxylic acid (prepn given) was treated with oxalic chloride, followed by the addition of 4-(4-methoxyphenyl)piperazine (prepn given) in the presence of pyridine to afford the piperazine II. II showed IC50 of <12 nM against PDE IV.

IT **223794-93-2P 479226-27-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT(Reactant or reagent)(intermediate; preparation of phenylpyridinecarbonylpiperazine derivs. as PDE IV inhibitors)

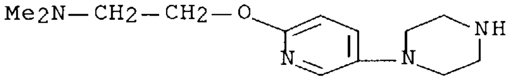
RN 223794-93-2 CAPLUS

CN Piperazine, 1-(5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



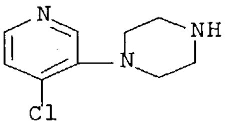
RN 479226-27-2 CAPLUS

CN Ethanamine, N,N-dimethyl-2-[[5-(1-piperazinyl)-2-pyridinyl]oxy]- (9CI) (CA INDEX NAME)

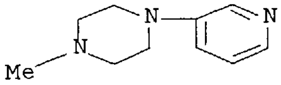


RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 9 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:884258 CAPLUS Full-text
DN 138:100350
TI Structure-Affinity Relationship Study on N-[4-(4-Arylpiperazin-1-yl)butyl]arylcarboxamides as Potent and Selective Dopamine D3 Receptor Ligands
AU Leopoldo, Marcello; Berardi, Francesco; Colabufo, Nicola A.; De Giorgio, Paola; Lacivita, Enza; Perrone, Roberto; Tortorella, Vincenzo
CS Dipartimento Farmaco-Chimico, Universita degli Studi di Bari, Bari, 70126, Italy
SO Journal of Medicinal Chemistry (2002), 45(26), 5727-5735
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 138:100350
AB The benzamide PB12 (N-[2-[4-(4-chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide) (1), already reported as potent and selective dopamine D4 receptor ligand, has been modified searching for structural features that could lead to D3 receptor affinity. Changes in the aromatic ring linked to N-1 piperazine ring led to the identification of 2-methoxyphenyl and 2,3-dichlorophenyl derivs. (compds. 6 and 13) displaying moderate D3 affinity (Ki = 145 and 31 nM, resp.). Intermediate alkyl chain elongation in compds. 1, 6, and 13 improved binding affinity for the D3 receptor and decreased the D4 affinity (compds. 18-26). Among these latter compds., the N-[4-[4-(2,3-dichlorophenyl)piperazin-1-yl]butyl]-3-methoxybenzamide (19) was further modified with the replacement or of the 2,3-dichlorophenyl moiety (compds. 27-30) or of the 3-methoxyphenyl ring (compds. 31-41). In this way, we identified several high-affinity D3 ligands (0.13 nM < Ki's < 4.97 nM) endowed with high selectivity over D2, D4, 5-HT1A, and α1 receptors. In addition, N-[4-[4-(2,3- dimethylphenyl)piperazin-1-yl]butyl]-3-methoxybenzamide (27) and N-[4-[4-(2,3-dichlorophenyl)piperazin-1-yl]butyl]-7-methoxy-2- benzofurancarboxamide (41) appear to be valuable candidates for positron emission tomog. (PET) because of their affinity values, lipophilicity properties, and liability of 11C labeling in the O-Me position.
IT **67980-90-9**, Piperazine, 1-(4-chloro-3-pyridinyl)-
223794-26-1, Piperazine, 1-(4-methyl-3-pyridinyl)-
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure-affinity relationship of N-[4-(4-Arylpiperazin-1-yl)butyl]arylcarboxamides as potent and selective D3 receptor ligands)
RN 67980-90-9 CAPLUS
CN Piperazine, 1-(4-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)

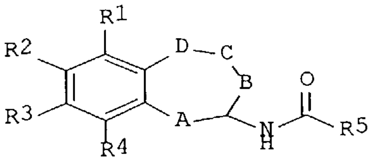


RN 223794-26-1 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)

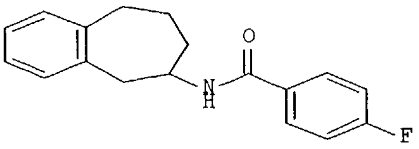


```
RE.CNT  38      THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 10 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:637637  CAPLUS Full-text
DN   137:185325
TI   Preparation of acylated 6,7,8,9-tetrahydro-5H-benzocycloheptenylamines
as
     stimulators of endothelial NO-synthase transcription
IN   Strobel, Hartmut; Wohlfart, Paulus
PA   Aventis Pharma Deutschland GmbH, Germany
SO   PCT Int. Appl., 101 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE           APPLICATION NO.   DATE
     ---------------     ----  --------       ---------------   --------
PI   WO 2002064546        A2   20020822       WO 2002-EP1449    20020212
     WO 2002064546        A3   20021107
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EE 200300370         A    20031015       EE 2003-370       20020212
     EP 1362027           A2   20031119       EP 2002-722069    20020212
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004518720        T2   20040624       JP 2002-564479    20020212
     US 2003008915        A1   20030109       US 2002-73203     20020213
     US 6759412           B2   20040706
     NO 2003003566        A    20031013       NO 2003-3566      20030812
PRAI EP 2001-102853       A    20010213
     WO 2002-EP1449       W    20020212
OS   MARPAT 137:185325
GI
```



I

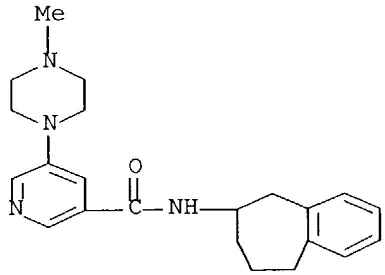


II

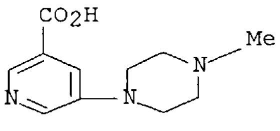
```
AB   Title compds. I [wherein R1 and R4 = independently H, (pseudo)halo, CF3,
     NO2, or (un)substituted alkyl, alkenyl, alkynyl, Ph, heteroaryl, amino,
     alkoxy, sulfamoyl, etc.; R2 and R3 = independently H, (pseudo)halo, OH,
     PhO, alkoxy, CF3, CN, NO2, or (un)substituted alkyl, amino, acylamino,
     etc.; A = CH2, CHOH, or CH(alkyl); B, C, and D = independently CH2 or
```

CH(alkyl); R5 = (un)substituted (hetero)aryl; and stereoisomers, mixts., or pharmaceutically acceptable salts thereof] were prepared as stimulators of endothelial NO-synthase (eNOS) transcription, which has a vasodilating effect and inhibits the aggregation of platelets, the adhesion of leukocytes to the endothelium, and the proliferation of intimal smooth muscle cells. For example, amidation of 4-fluorobenzoic acid chloride with 6,7,8,9-tetrahydro-5H-benzocyclohepten-6-ylamine in the presence of TEA in dioxane afforded II. The latter activated eNOS transcription in primary human umbilical vein cord endothelial cells (HUVEC) with EC50 of 0.02 μM. I are useful for the treatment of cardiovascular diseases, stable or unstable angina pectoris, coronary heart disease, Prinzmetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, thrombosis, peripheral artery occlusive disease, endothelial dysfunction, atherosclerosis, restenosis, endothelial damage after PTCA, hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension, chronic glomerulonephritis, erectile dysfunction, ventricular arrhythmia, diabetes, diabetes complications, nephropathy, retinopathy, angiogenesis, asthma bronchial, chronic renal failure, cirrhosis of the liver, osteoporosis, or restricted memory performance or for a restricted ability to learn, or the lowering of cardiovascular risk of postmenopausal women or after intake of contraceptives (no data).

IT **450367-28-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(eNOS transcription stimulator; preparation of acylated tetrahydrobenzocycloheptenylamines as stimulators of endothelial NO-synthase transcription)
RN 450367-28-9 CAPLUS
CN 3-Pyridinecarboxamide, 5-(4-methyl-1-piperazinyl)-N-(6,7,8,9-tetrahydro-5H-benzocyclohepten-6-yl)- (9CI) (CA INDEX NAME)



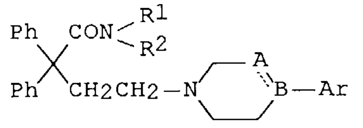
IT **450368-31-7**, 5-(4-Methylpiperazin-1-yl)nicotinic acid
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of acylated tetrahydrobenzocycloheptenylamines as stimulators of endothelial NO-synthase transcription)
RN 450368-31-7 CAPLUS
CN 3-Pyridinecarboxylic acid, 5-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



L23 ANSWER 11 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:293621 CAPLUS Full-text
DN 136:325561
TI Preparation of 4-pyridyl or 4-(1-piperazinyl)-2,2-diphenylbutanamide derivatives as μ-opioid agonists and medicines containing the same
IN Okada, Tomomi; Komoto, Teruo; Sato, Susumu; Oka, Tetsuo; Sakamoto, Takao;
Kanamaru, Yoshihiko; Mogi, Kinichi; Morimoto, Shinichi; Umehara, Norimitsu; Kamei, Junzo
PA SSP Co., Ltd., Japan
SO PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

```
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   WO 2002030896     A1    20020418      WO 2001-JP8982    20011012
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001094240     A5    20020422      AU 2001-94240     20011012
     EP 1325912        A1    20030709      EP 2001-974820    20011012
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2004034104     A1    20040219      US 2003-399135    20030414
PRAI JP 2000-311926    A     20001012
     JP 2000-398474    A     20001227
     WO 2001-JP8982    W     20011012
```

OS MARPAT 136:325561
GI



I

AB 2,2-Diphenylbutanamide derivs. represented by the general formula (I) or salts thereof [wherein A is (CH2)n (wherein n is 1 or 2) or methine (CH); when A is CH2, B is methine or nitrogen and the bond between A and B is single; when A is (CH2)2, B is nitrogen and the bond between A and B is single; and when A is methine, B is quaternary carbon and the bond between A and B is double; R1 and R2 are each independently hydrogen, lower alkyl, or cycloalkyl, or alternatively R1 and R2 together with the nitrogen atom adjacent thereto may form a heterocycle; and Ar is optionally substituted Ph, a bicyclic aromatic ring group, a mono- or bi-cyclic heterocyclic group, or a fluorene group] are prepared These derivs. exhibit excellent μ-opioid agonism and analgesic activity against neurogenic pain and are useful as drugs including peripherally acting analgesic and neurogenic pain controller. Thus, 0.5 g 2-bromoethyl acetate and 0.4 g K2CO3 were added to a solution of 1.1 g 4-

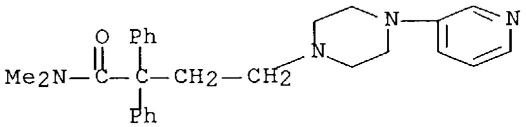
[4-(2-hydroxyphenyl)piperazin-1-yl]-N,N- dimethyl-2,2-diphenylbutanamide in 20 mL DMF and stirred at room temperature for 12 h to give 51.0% 2-[2-[4-[4-(dimethylamino)-3,3-diphenyl-4- oxobutyl]piperazin-1-yl]phenoxy]ethyl acetate which (560 mg) was dissolved in 5 mL MeOH, treated with 5 mL 1 N aqueous NaOH, and stirred at 50° for 1 h to give 85.9% 4-[4-[2-(2-hydroxyethoxy)phenyl]piperazin-1-yl]-N,N- dimethyl-2,2-diphenylbutanamide (II). In an opioid receptor agonist assay (Eur. J. Pharmacol., 77;137-141, 1982), II in vitro inhibited the elec. evoked contractions of the guinea pig ileum with 20-times the potency of the selective μ-opioid agonist DAMGO ([D-Ala2, N-MePHe4, Gly5-ol]-enkephalin).

IT **386214-47-7P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of 4-pyridyl or (1-piperazinyl)phenylbutanamide derivs. as μ-opioid agonists and analgesics)

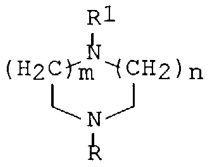
RN 386214-47-7 CAPLUS

CN 1-Piperazinebutanamide, N,N-dimethyl-α,α-diphenyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)

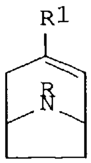


RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 12 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:293427  CAPLUS Full-text
DN   136:325574
TI   Preparation of piperazine, homopiperazine, and 8-azabicyclo[3.2.1]oct-2-
     ene, and 3,9-diazabicyclo[4.2.1]nonane derivatives for treatment of
     affective disorders by the combined action of a nicotinic receptor
     agonist and a monoaminergic substance
IN   Olsen, Gunnar M.; Peters, Dan; Nielsen, Elsebet Ostergaard
PA   Neurosearch A/S, Den.
SO   PCT Int. Appl., 31 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ---------------     ----  --------      ---------------   --------
PI   WO 2002030405        A2   20020418      WO 2001-DK661     20011010
     WO 2002030405        A3   20020906
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2001095436        A5   20020422      AU 2001-95436     20011010
     EP 1358177           A2   20031105      EP 2001-976043    20011010
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004510813        T2   20040408      JP 2002-533848    20011010
     US 2004092508        A1   20040513      US 2003-380653    20030317
PRAI DK 2000-1535         A    20001013
     US 2000-242146P      P    20001023
     WO 2001-DK661        W    20011010
OS   MARPAT 136:325574
GI
```



I



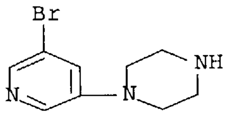
II

```
AB    This invention relates to use of the combined action of a nicotinic
      acetylcholine receptor agonist and a monoamine reuptake inhibitor for
      the treatment of affective disorders including depression, anxiety,
      obsessive compulsive disorder (OCD), panic disorder, or pain, as well as
      to pharmaceutical compns. comprising these substances and chemical
      substances for use according to the invention.  The chemical substances
      are represented by piperazine and homopiperazine derivs. (I; n = 1,2,3;
      m = 0,1,2; R = H, alkyl, cycloalkyl, cycloalkylalkyl, alkoxy, acyl,
      benzyl; R1 = 5-bromo-3-pyridyl, 6-chloro-3-pyridyl, 6-bromo-5-methoxy-3-
      pyridyl, 6-bromo-3-pyridyl, 6-bromo-5-chloro-3-pyridyl, 5,6-dibromo-3-
      pyridyl, etc.) and 8-azabicyclo[3.2.1]oct-2-ene derivs. (II; R = H,
```

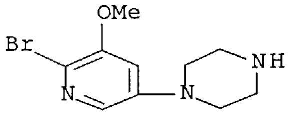
alkyl, alkenyl, cycloalkyl, cyanoalkyl, Ph, naphthyl, benzyl; R1 = CHO, alkanoyl, cycloalkanoyl, carbamoyl, furanyl, thienyl, pyrrolyl, oxazolyl, isoxazolyl, imidazolyl, pyridyl, pyrimidinyl, thiazolyl, naphthyl, indolyl, benzofuranyl, etc.). Thus, 1-(6-Chloro-3-pyridyl)piperazine (III) (0.3, 1, 3, 10 mg/kg s.c.) was tested in the mouse forced swim test which is considered predictive of a potential antidepressant pharmacol. effect and it did not affect forced swimming with a 30 min pretreatment. However, the combination of venlafaxine and III (1+3; 3+3; 10+1; 10+3 mg/kg s.c.) significantly increased the forced swimming in NMRI mice.

IT **412347-30-9P**, 1-(5-Bromo-3-pyridyl)piperazine **412347-32-1P**, 1-(6-Bromo-5-methoxy-3-pyridyl)piperazine **412347-39-8P**, 1-(6-Bromo-3-pyridyl)piperazine **412347-41-2P**, 1-(6-Bromo-5-chloro-3-pyridyl)piperazine **412347-44-5P**, 1-(5,6-Dibromo-3-pyridyl)piperazine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(intermediate; preparation of piperazine, homopiperazine, azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for treatment of affective disorders)

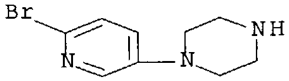
RN 412347-30-9 CAPLUS
CN Piperazine, 1-(5-bromo-3-pyridinyl)- (9CI) (CA INDEX NAME)



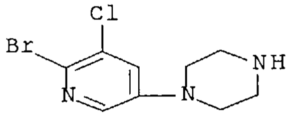
RN 412347-32-1 CAPLUS
CN Piperazine, 1-(6-bromo-5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



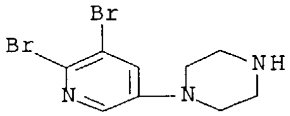
RN 412347-39-8 CAPLUS
CN Piperazine, 1-(6-bromo-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 412347-41-2 CAPLUS
CN Piperazine, 1-(6-bromo-5-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



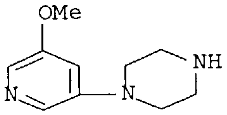
RN 412347-44-5 CAPLUS
CN Piperazine, 1-(5,6-dibromo-3-pyridinyl)- (9CI) (CA INDEX NAME)



IT **223794-94-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(intermediate; preparation of piperazine, homopiperazine, azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for treatment of affective disorders)
RN 223794-94-3 CAPLUS
CN Piperazine, 1-(5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

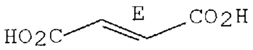
CRN 223794-93-2
CMF C10 H15 N3 O



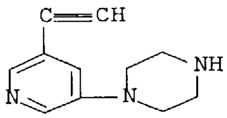
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



IT **412347-53-6P**, 1-(5-Ethynyl-3-pyridyl)piperazine
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of piperazine, homopiperazine, azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for treatment of affective disorders)
RN 412347-53-6 CAPLUS
CN Piperazine, 1-(5-ethynyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



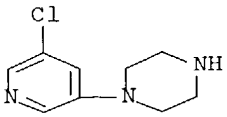
IT **223794-96-5P** **412347-31-0P** **412347-33-2P**
412347-37-6P, 1-(6-Iodo-5-methoxy-3-pyridyl)piperazine
412347-38-7P **412347-40-1P** **412347-42-3P**
412347-45-6P **412347-50-3P**, 1-(6-Bromo-5-ethynyl-3-pyridyl)piperazine **412347-51-4P** **412347-55-8P**,
1-(6-Chloro-5-bromo-3-pyridyl)piperazine **412347-56-9P**
412347-59-2P, 1-(5,6-Dichloro-3-pyridyl)piperazine
412347-60-5P **412347-61-6P**, 1-(6-Chloro-3-pyridyl)piperazine dihydrochloride **412347-64-9P**,
1-(6-Chloro-5-methoxy-3-pyridyl)piperazine **412347-65-0P**
412348-20-0P, 1-(6-Phenyl-3-pyridyl)piperazine
412348-21-1P **412348-36-8P**, 1-(5-Chloro-6-phenyl-3-pyridyl)piperazine **412348-37-9P** **412348-55-1P**
412349-03-2P, 1-(6-Chloro-3-pyridyl)piperazine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(Uses) (preparation of piperazine, homopiperazine,
azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for
treatment of affective disorders)

RN 223794-96-5 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)
(CA INDEX NAME)

CM 1

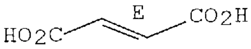
CRN 223794-95-4
CMF C9 H12 Cl N3



CM 2

CRN 110-17-8
CMF C4 H4 O4

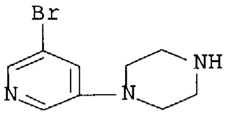
Double bond geometry as shown.



RN 412347-31-0 CAPLUS
CN Piperazine, 1-(5-bromo-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)
(CA INDEX NAME)

CM 1

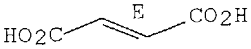
CRN 412347-30-9
CMF C9 H12 Br N3



CM 2

CRN 110-17-8
CMF C4 H4 O4

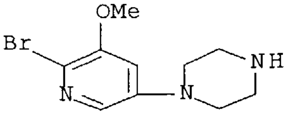
Double bond geometry as shown.



RN 412347-33-2 CAPLUS
CN Piperazine, 1-(6-bromo-5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate
(1:1)(9CI) (CA INDEX NAME)

CM 1

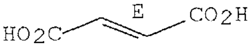
CRN 412347-32-1
CMF C10 H14 Br N3 O



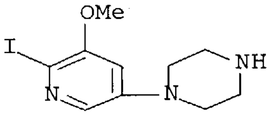
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



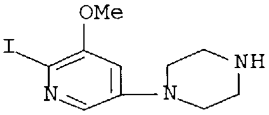
RN 412347-37-6 CAPLUS
CN Piperazine, 1-(6-iodo-5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 412347-38-7 CAPLUS
CN Piperazine, 1-(6-iodo-5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

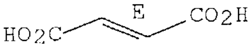
CRN 412347-37-6
CMF C10 H14 I N3 O



CM 2

CRN 110-17-8
CMF C4 H4 O4

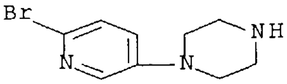
Double bond geometry as shown.



RN 412347-40-1 CAPLUS
CN Piperazine, 1-(6-bromo-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

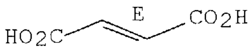
CRN 412347-39-8
CMF C9 H12 Br N3



CM 2

CRN 110-17-8
CMF C4 H4 O4

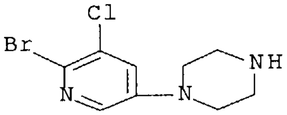
Double bond geometry as shown.



RN 412347-42-3 CAPLUS
CN Piperazine, 1-(6-bromo-5-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

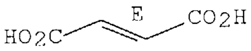
CRN 412347-41-2
CMF C9 H11 Br Cl N3



CM 2

CRN 110-17-8
CMF C4 H4 O4

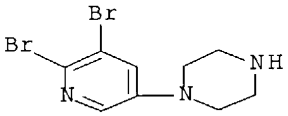
Double bond geometry as shown.



RN 412347-45-6 CAPLUS
CN Piperazine, 1-(5,6-dibromo-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

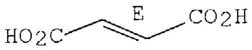
CRN 412347-44-5
CMF C9 H11 Br2 N3



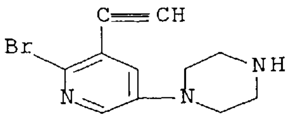
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



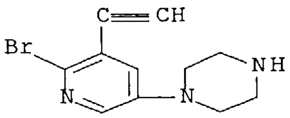
RN 412347-50-3 CAPLUS
CN Piperazine, 1-(6-bromo-5-ethynyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 412347-51-4 CAPLUS
CN Piperazine, 1-(6-bromo-5-ethynyl-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

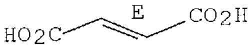
CRN 412347-50-3
CMF C11 H12 Br N3



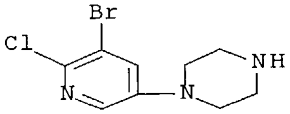
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



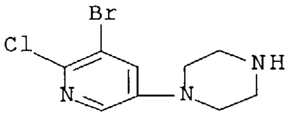
RN 412347-55-8 CAPLUS
CN Piperazine, 1-(5-bromo-6-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 412347-56-9 CAPLUS
CN Piperazine, 1-(5-bromo-6-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

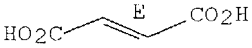
CRN 412347-55-8
CMF C9 H11 Br Cl N3



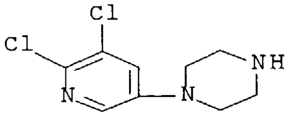
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



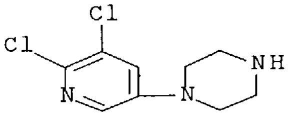
RN 412347-59-2 CAPLUS
CN Piperazine, 1-(5,6-dichloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 412347-60-5 CAPLUS
CN Piperazine, 1-(5,6-dichloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)(CA INDEX NAME)

CM 1

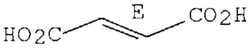
CRN 412347-59-2
CMF $C_9 H_{11} Cl_2 N_3$



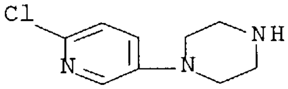
CM 2

CRN 110-17-8
CMF $C_4 H_4 O_4$

Double bond geometry as shown.

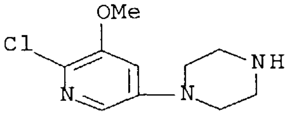


RN 412347-61-6 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

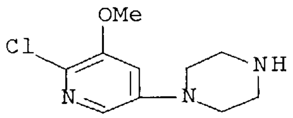
RN 412347-64-9 CAPLUS
CN Piperazine, 1-(6-chloro-5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



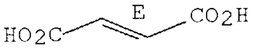
RN 412347-65-0 CAPLUS
CN Piperazine, 1-(6-chloro-5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1)(9CI) (CA INDEX NAME)

CM 1

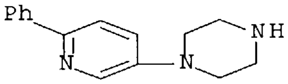
```
     CRN  412347-64-9
     CMF  C10 H14 Cl N3 O
```



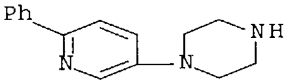
```
     CM   2

     CRN  110-17-8
     CMF  C4 H4 O4

Double bond geometry as shown.
```



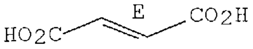
```
RN   412348-20-0  CAPLUS
CN   Piperazine, 1-(6-phenyl-3-pyridinyl)- (9CI)  (CA INDEX NAME)
```



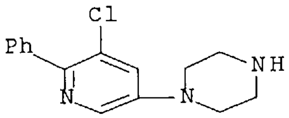
```
RN   412348-21-1  CAPLUS
CN   Piperazine, 1-(6-phenyl-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)
     (CA INDEX NAME)

     CM   1

     CRN  412348-20-0
     CMF  C15 H17 N3
```



```
     CM   2

     CRN  110-17-8
     CMF  C4 H4 O4

Double bond geometry as shown.
```



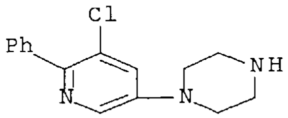
```
RN   412348-36-8  CAPLUS
CN   Piperazine, 1-(5-chloro-6-phenyl-3-pyridinyl)- (9CI)  (CA INDEX NAME)
```



```
RN   412348-37-9  CAPLUS
CN   Piperazine, 1-(5-chloro-6-phenyl-3-pyridinyl)-, (2E)-2-butenedioate
     (1:1) (9CI)  (CA INDEX NAME)
```

CM 1

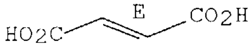
CRN 412348-36-8
CMF C15 H16 Cl N3



CM 2

CRN 110-17-8
CMF C4 H4 O4

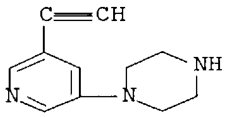
Double bond geometry as shown.



RN 412348-55-1 CAPLUS
CN Piperazine, 1-(5-ethynyl-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

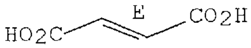
CRN 412347-53-6
CMF C11 H13 N3



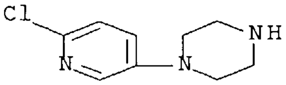
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

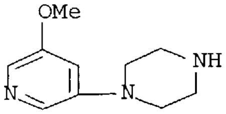


RN 412349-03-2 CAPLUS
CN Piperazine, 1-(6-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)

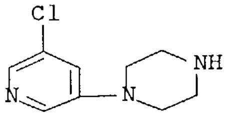


IT **223794-93-2**, 1-(5-Methoxy-3-pyridyl)piperazine **223794-95-4**, 1-(5-Chloro-3-pyridyl)piperazine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperazine, homopiperazine, azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for treatment of affective disorders)

RN 223794-93-2 CAPLUS
CN Piperazine, 1-(5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



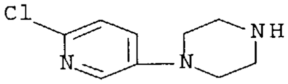
RN 223794-95-4 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



IT **412349-26-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic composition; preparation of piperazine, homopiperazine, azabicyclo[3.2.1]octene, and diazabicyclo[4.2.1]nonane derivs. for treatment of affective disorders)
RN 412349-26-9 CAPLUS
CN Cyclohexanol, 1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]-, mixt. with 1-(6-chloro-3-pyridinyl)piperazine (9CI) (CA INDEX NAME)

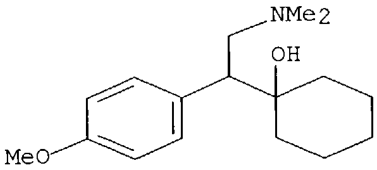
CM 1

CRN 412349-03-2
CMF C9 H12 Cl N3

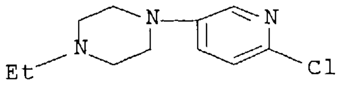


CM 2

CRN 93413-69-5
CMF C17 H27 N O2

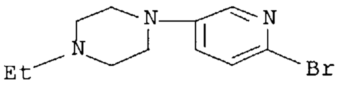


```
L23  ANSWER 13 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2002:158405  CAPLUS Full-text
DN   136:200113
TI   3-Cyanoquinolines, 3-cyano-1,6-naphthyridines, and 3-cyano-1,7-
     naphthyridines as protein kinase inhibitors
IN   Boschelli, Diane Harris; Wang, Yanong; Boschelli, Frank Charles; Berger,
     Dan Maarten; Zhang, Nan; Powell, Dennis William; Ye, Fei; Yamashita,
     Ayako; Demorin, Frenel Fils; Wu, Biqi; Tsou, Hwei-ru; Overbeek-Klumpers,
     Elsebe Geraldine; Wissner, Allan
PA   American Home Products Corporation, USA; Wyeth
SO   U.S. Pat. Appl. Publ., 172 pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   US 2002026052      A1   20020228      US 2001-820070    20010328
     US 6521618         B2   20030218
     US 6689772         B1   20040210      US 2002-318213    20021212
PRAI US 2000-219322P    P    20000328
     US 2001-820070     A3   20010328
OS   MARPAT 136:200113
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

AB    Title compds. I [X = N(H) or substituted derivs., O, SO0-2; n = 0-1; A =
      divalent (un)substituted alkyl, C(O), C(O)-alkyl, alkyl-C(O),
      cycloalkyl, or absent; T, Z = C, N provided that both T and Z are not N;
      R1 = cycloalkyl, 5-6 atom (hetero)aryl ring containing 0-4 heteroatoms,
      8-20 atom bicyclic heteroaryl ring containing 1-4 heteroatoms, etc.;
      R2a-c = H, aryl, CH2-aryl, O-aryl, SO0-2-aryl, NO2, SH, etc.; R3 =
      alkenyl, alkynyl, (hetero)aryl; R4 = (un)substituted alkyl, alkenyl,
      alkynyl, (hetero)aryl] were prepared  Over 500 synthetic examples were
      disclosed, including some combinatorial prepns., and addnl. reference
      examples.  E.g., 4-[(4-bromo-2-thienyl)methyl]morpholine reacted with
      bis(pinacolato)diboron [DMSO, PdCl2(dppf), KOAc] to give dioxaborolane
      II. II was coupled to 7-bromo-4-[3-chloro-4-[(1-methyl-1H-imidazol-2-
      yl)sulfanyl]anilino]-3-quinolinecarbonitrile [preparation given;
      diglyme, Pd(PPh3)4, NaHCO3] to yield invention compound III as a yellow
      solid after purification  III had IC50 = 6.0 nM for Raf1 kinase and
      inhibited the human adenocarcinoma CaCo-2 cell line with IC50 = 1.9,
      0.78 (2 trials).  I are useful as antineoplastic agents, and in the
      treatment of osteoporosis and polycystic kidney disease.
IT    364794-24-1P 364794-25-2P
      RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
      RACT (Reactant or reagent) (intermediate; preparation of cyanoquinolines
      and cyanonaphthyridines as protein kinase inhibitors)
RN    364794-24-1  CAPLUS
CN    Piperazine, 1-(6-chloro-3-pyridinyl)-4-ethyl- (9CI)  (CA INDEX NAME)
```

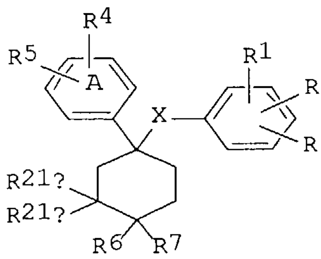


```
RN    364794-25-2  CAPLUS
```

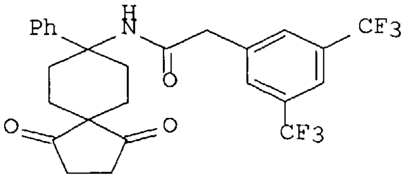
CN   Piperazine, 1-(6-bromo-3-pyridinyl)-4-ethyl- (9CI)   (CA INDEX NAME)



```
L23  ANSWER 14 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:851115  CAPLUS Full-text
DN   136:5907
TI   Synthesis of aryl-amido-cyclohexane derivatives and their use as NK-1
     receptor antagonists
IN   Castro Pineiro, Jose Luis; Dinnell, Kevin; Elliott, Jason Matthew;
     Hollingworth, Gregory John; Shaw, Duncan Edward; Swain, Christopher John
PA   Merck Sharp & Dohme Limited, UK
SO   PCT Int. Appl., 199 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2001087838      A1   20011122      WO 2001-GB2145   20010516
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,
             RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1286967         A1   20030305      EP 2001-929829   20010516
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2003533509      T2   20031111      JP 2001-584234   20010516
     US 2003236250      A1   20031225      US 2002-276127   20021113
PRAI GB 2000-12240      A    20000519
     WO 2001-GB2145     W    20010516
OS   MARPAT 136:5907
GI
```



I



II

AB Title compds. I [ring A = Ph or pyridyl; X = linker selected from amido(carbonyl), amino, ester, ether; R1 = OH, (fluoro)alkyl, alkenyl, cycloalkyl, (fluoro)alkoxy, etc.; R2 = H, halo, alkyl, alkoxy or R1-2 with the atom to which they are attached, may form a 5 - 6 membered ring; R3 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, cycloalkyl, CN, etc. or R3 = 5 - 6 membered heterocyclic ring; R4 = H, halo, (fluoro)alkyl, (fluoro)alkoxy, OH, NO2, CN, etc.; R5 = H, halo, (fluoro)alkyl, alkoxy; R6 = H, OH, alkyl; R7 = H, OH, alkylamino, alkylcarboxy, carbocyclyl, C-linked heterocyclyl or heteroaryl or R6-7 together represent :O, :CH-ester, ketal; R21a = H, halo, OH; R21b = H, or R21a-21b = F or together represent :O] were prepared Over 300 synthetic examples were disclosed. For instance, 3,5-bis(trifluoromethyl)benzeneacetic acid was converted to the acid chloride derivative (CH2Cl2, ClCOCOCl, DMF, room temperature, 1 h), and used to acylate 1,4-dioxo-8-phenylspiro[4.5]decan-8-amine (preparation given, dichloroethane, Et3N, room temperature) to give II as a brown gum in quant. yield. I are neurokinin 1 (NK-1) receptor antagonists (no data). Compds. I are of particular use in the treatment or prevention of depression, anxiety, pain, inflammation, migraine, emesis or postherpetic neuralgia.

IT **374792-48-0P**

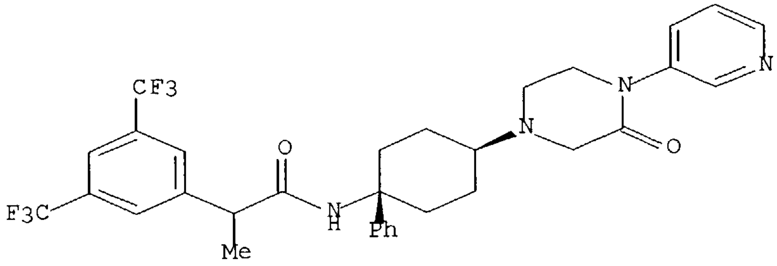
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug; synthesis of aryl-amido-cyclohexane derivs. and use as NK-1 receptor antagonists)

RN 374792-48-0 CAPLUS

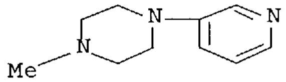
CN Benzeneacetamide, α-methyl-N-[trans-4-[3-oxo-4-(3-pyridinyl)-1-piperazinyl]-1-phenylcyclohexyl]-3,5-bis(trifluoromethyl)- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 15 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:731861 CAPLUS Full-text
DN 136:14987
TI Structure-Affinity Relationships of a Unique Nicotinic Ligand:
N1-Dimethyl-N4-phenylpiperazinium Iodide (DMPP)
AU Romanelli, Maria Novella; Manetti, Dina; Scapecchi, Serena; Borea, Pier
Andrea; Dei, Silvia; Bartolini, Alessandro; Ghelardini, Carla;
Gualtieri,
Fulvio; Guandalini, Luca; Varani, Katia
CS Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence,
50121, Italy
SO Journal of Medicinal Chemistry (2001), 44(23), 3946-3955
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB DMPP is a well-known nicotinic agonist that does not fit any proposed pharmacophore for nicotinic binding and represents a unique ligand among the hundreds of nicotinic agonists studied in the past decades. A systematic modulation of the chemical structure of DMPP, aimed to establish its structure-affinity relationships, is reported. The research has allowed to identify mols. with affinities for α4β2 receptors in the low nanomolar range, some 2 orders of magnitude lower than the lead compound The agonistic properties of the most interesting compds. have been assessed by measuring their analgesic activity on mice (hot-plate test). Another result of the research was the identification of DMPP analogs with Ki = 90 nM and 180 nM, that maintain affinity for the central nicotinic receptor when the ammonium function is changed into an aminic one and are therefore possible leads for drug development in neurodegenerative diseases.
IT **223794-26-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(structure-activity relationships of a nicotinic ligand, DMPP)
RN 223794-26-1 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



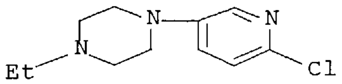
RE.CNT 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 16 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:730706  CAPLUS Full-text
DN   135:288703
TI   3-Cyanoquinolines, 3-cyano-1,6-naphthyridines, and 3-cyano-1,7-
     naphthyridines as protein kinase inhibitors
IN   Boschelli, Diane Harris; Wang, Yanong; Boschelli, Frank Charles; Berger,
     Dan Maarten; Zhang, Nan; Powell, Dennis William; Ye, Fei; Yamashita,
     Ayako; Demorin, Frenel Fils; Wu, Biqi; Tsou, Hwei-ru; Overbeek-klumpers,
     Elsebe Geraldine; Wissner, Allan
PA   American Home Products Corporation, USA
SO   PCT Int. Appl., 448 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 2001072711      A1   20011004       WO 2001-US9966   20010328
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1268431         A1   20030102       EP 2001-924407   20010328
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     BR 2001009650      A    20030422       BR 2001-9650     20010328
     JP 2003528857      T2   20030930       JP 2001-570624   20010328
PRAI US 2000-535843     A    20000328
     WO 2001-US9966     W    20010328
OS   MARPAT 135:288703
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

AB    Title compds. I [X = N(H) or substituted derivs., O, SO0-2; n = 0-1; A =
      divalent (un)substituted alkyl, C(O), C(O)-alkyl, alkyl-C(O),
      cycloalkyl, or absent; T, Z = C, N provided that both T and Z are not N;
      R1 = cycloalkyl, 5-6 atom (hetero)aryl ring containing 0-4 heteroatoms,
      8-20 atom bicyclic heteroaryl ring containing 1-4 heteroatoms, etc.;
      R2a-c = H, aryl, CH2-aryl, O-aryl, SO0-2-aryl, NO2, SH, etc.; R3 =
      alkenyl, alkynyl, (hetero)aryl; R4 = (un)substituted alkyl, alkenyl,
      alkynyl, (hetero)aryl] were prepared  Over 500 synthetic examples were
      disclosed, including some combinatorial prepns., and addnl. reference
      examples.  E.g., 4-[(4-bromo-2-thienyl)methyl]morpholine reacted with
      bis(pinacolato)diboron [DMSO, PdCl2(dppf), KOAc] to give dioxaborolane
      II. II was coupled to 7-bromo-4-[3-chloro-4-[(1-methyl-1H-imidazol-2-
      yl)sulfanyl]anilino]-3-quinolinecarbonitrile [preparation given;
      diglyme, Pd(PPh3)4, NaHCO3] to yield invention compound III as a yellow
      solid after purification  III had IC50 = 6.0 nM for Raf1 kinase and
      inhibited the human adenocarcinoma CaCo-2 cell line with IC50 = 1.9,
      0.78 (2 trials).  I are useful as antineoplastic agents, and in the
      treatment of osteoporosis and polycystic kidney disease.
```

IT **364794-24-1P 364794-25-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(intermediate; preparation of cyanoquinolines and cyanonaphthyridines as protein kinase inhibitors)

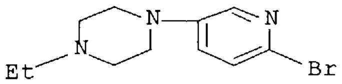
RN 364794-24-1 CAPLUS

CN Piperazine, 1-(6-chloro-3-pyridinyl)-4-ethyl- (9CI) (CA INDEX NAME)



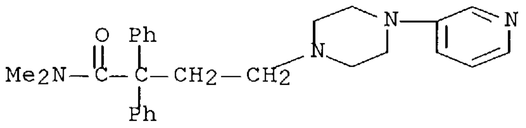
RN 364794-25-2 CAPLUS

CN Piperazine, 1-(6-bromo-3-pyridinyl)-4-ethyl- (9CI) (CA INDEX NAME)



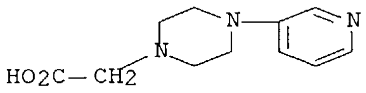
RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 17 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:724747 CAPLUS Full-text
DN 136:79260
TI New μ-opioid receptor agonists with piperazine moiety
AU Komoto, Teruo; Okada, Tomomi; Sato, Susumu; Niino, Yasuhiro; Oka, Tetsuo;
Sakamoto, Takao
CS Central Research Labs., SSP Co., Ltd., Chiba, 286-8511, Japan
SO Chemical & Pharmaceutical Bulletin (2001), 49(10), 1314-1320
CODEN: CPBTAL; ISSN: 0009-2363
PB Pharmaceutical Society of Japan
DT Journal
LA English
AB New μ-opioid receptor (MOR) agonists containing piperazine and homopiperazine moieties in the structures were synthesized and their affinities to and agonist potencies on MOR were evaluated. Among the synthesized compds., 4-[4-(2-methoxyphenyl)piperazin-1-yl]-N,N-dimethyl-2,2-diphenylbutanamide showed the highest affinity to the human MOR expressed in Chinese hamster ovary (CHO)-K1 cells, and the highest agonist potency on the MOR in isolated guinea-pig ileum preparation
IT **386214-47-7P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(new μ-opioid receptor agonists with piperazine moiety)
RN 386214-47-7 CAPLUS
CN 1-Piperazinebutanamide, N,N-dimethyl-α,α-diphenyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



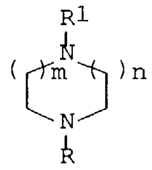
RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 18 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2001:453023  CAPLUS Full-text
DN   135:46207
TI   Preparation of heterocyclic derivatives as anticancer agents
IN   Suzuki, Toshiyuki; Aoki, Tomiyoshi
PA   Nippon Shinyaku Co., Ltd., Japan
SO   PCT Int. Appl., 41 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  ---------      ---------------  ---------
PI   WO 2001044195     A1    20010621       WO 2000-JP8781   20001213
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2001018873     A5    20010625       AU 2001-18873    20001213
     EP 1238974        A1    20020911       EP 2000-981657   20001213
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2003022884     A1    20030130       US 2002-149622   20020612
PRAI JP 1999-354101    A     19991214
     JP 2000-202393    A     20000704
     WO 2000-JP8781    W     20001213
OS   MARPAT 135:46207
AB    The title compds. ABDE [A is heteroaryl or an oxide thereof; B is
      ethenylene; D is optionally substituted phenylene; and E is a group of
      general formula N(COR)SO2G (G is optionally substituted phenyl; and R is
      heteroaryl, heteroarylmethyl), etc.] are prepared  A course of 5
      injections of (E)-4-(2-(2-(N-(4-methoxybenzenesulfonyl)-N-(4-(2-
      pyridyl)piperazino)acetylamino)phenyl)ethenyl)pyridine 1-oxide
      dihydrochloride at 50 mg/kg i.v. gave 80% inhibition of tumor in mice.
      Formulations are given.
IT   345206-93-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of heterocyclic derivs. as anticancer agents)
RN   345206-93-1  CAPLUS
CN   1-Piperazineacetic acid, 4-(3-pyridinyl)- (9CI)  (CA INDEX NAME)
```

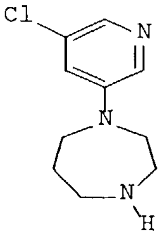


```
RE.CNT  11     THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 19 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:772619  CAPLUS Full-text
DN   133:321908
TI   Heteroaryl diazacycloalkanes, their preparation, and their use as
     nicotinic acetylcholine receptor ligands
IN   Nielsen, Simon Feldbaek; Peters, Dan; Nielsen, Elsebet Ostergaard;
     Olsen, Gunnar M.
PA   Neurosearch A/S, Den.
SO   PCT Int. Appl., 70 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE           APPLICATION NO.   DATE
     ---------------    ----  --------       ---------------   --------
PI   WO 2000064885       A1   20001102       WO 2000-DK202     20000419
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2000041006       A5   20001110       AU 2000-41006     20000419
     NZ 514021           A    20010928       NZ 2000-514021    20000419
     EP 1175416          A1   20020130       EP 2000-920421    20000419
     EP 1175416          B1   20030716
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002543070       T2   20021217       JP 2000-614237    20000419
     AT 245153           E    20030815       AT 2000-920421    20000419
     US 2002045618       A1   20020418       US 2001-934531    20010823
PRAI DK 1999-571         A    19990426
     DK 1999-1504        A    19991020
     WO 2000-DK202       W    20000419
OS   MARPAT 133:321908
GI
```



I



II

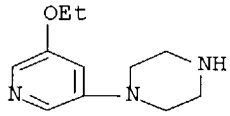
```
AB   The invention relates to novel heteroaryl diazacycloalkane derivs. I and
     their enantiomers, N-oxides, salts, and/or labeled forms [wherein: n =
     1, 2, 3; m = 0, 1, 2; R = H, alkyl, cycloalkyl, cycloalkylalkyl,
     alkenyl, alkynyl, aralkyl, alkoxypyridyl, alkenyloxypyridyl, or bridging
     moiety to form a dimer; R1 = (un)substituted monocyclic 5- or 6-membered
     heterocyclyl or bicyclic heterocyclyl; or R = R1 = (un)substituted
     monocyclic 5- or 6-membered heterocyclyl].  The compds. are cholinergic
```

ligands at nicotinic acetylcholine receptors, and may be useful for the treatment of a diversity of diseases and disorders, e.g., those related to the CNS cholinergic system, smooth muscle contraction, the endocrine system, neurodegeneration, inflammation, pain, and substance abuse withdrawal symptoms. A large number of compds., mostly homopiperazine derivs., were prepared and/or claimed. For instance, neat reaction of 3,5-dichloropyridine with homopiperazine at 150° gave title compound II in 40% yield. Similar compds. inhibited binding of 3H-epibatidine to rat brain nicotinic receptors with IC50 values as low as 0.001 μM.

IT **223795-11-7P**, 1-(5-Ethoxy-3-pyridyl)piperazine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of heteroaryldiazacycloalkanes as nicotinic acetylcholine receptor ligands)

RN 223795-11-7 CAPLUS

CN Piperazine, 1-(5-ethoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



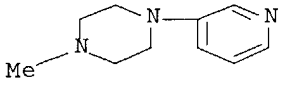
IT **223794-27-2P**, 4-Methyl-1-(3-pyridyl)piperazine fumaric acid salt **223795-12-8P**, 1-(5-Ethoxy-3-pyridyl)piperazine fumaric acid salt **223795-40-2P**, 1-(5-Ethoxy-3-pyridyl)-4-ethylpiperazine **223795-41-3P**, 1-(5-Ethoxy-3-pyridyl)-4-ethylpiperazine fumaric acid salt **303159-71-9P**, 1-(5-Pentyloxy-3-pyridyl)piperazine **303159-75-3P**, 1-[5-(trans-Hex-2-en-1-yloxy)-3-pyridyl]piperazine **303159-77-5P**, 1-(5-Methoxy-3-pyridyl)-4-ethylpiperazine **303159-79-7P**, 4-Methyl-1-(5-propyloxy-3-pyridyl)piperazine **303160-85-2P**, 1-(5-Pentyloxy-3-pyridyl)-4-methylpiperazine fumaric acid salt **303160-87-4P**, 1-[5-(trans-Hex-2-en-1-yloxy)-3-pyridyl]-4-methylpiperazine fumaric acid salt **303160-90-9P**, 1-(5-Methoxy-3-pyridyl)-4-ethylpiperazine fumaric acid salt **303160-92-1P**, 4-Ethyl-1-(5-propyloxy-3-pyridyl)piperazine fumaric acid salt
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of heteroaryldiazacycloalkanes as nicotinic acetylcholine receptor ligands)

RN 223794-27-2 CAPLUS

CN Piperazine, 1-methyl-4-(3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

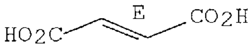
CRN 223794-26-1
CMF $C_{10}H_{15}N_3$



CM 2

CRN 110-17-8
CMF C4 H4 O4

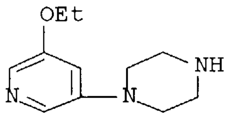
Double bond geometry as shown.



RN 223795-12-8 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

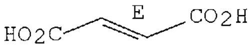
CRN 223795-11-7
CMF C11 H17 N3 O



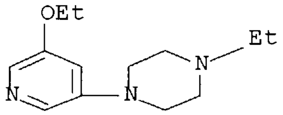
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



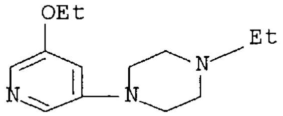
RN 223795-40-2 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-ethyl- (9CI) (CA INDEX NAME)



RN 223795-41-3 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-ethyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

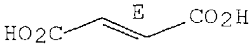
CRN 223795-40-2
CMF C13 H21 N3 O



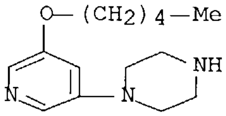
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

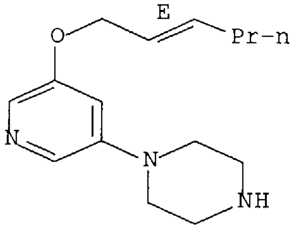


RN 303159-71-9 CAPLUS
CN Piperazine, 1-[5-(pentyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

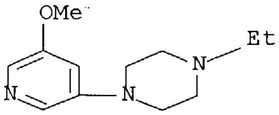


RN 303159-75-3 CAPLUS
CN Piperazine, 1-[5-[(2E)-2-hexenyloxy]-3-pyridinyl]- (9CI) (CA INDEX NAME)

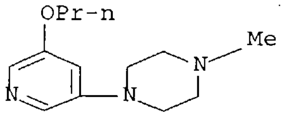
Double bond geometry as shown.



RN 303159-77-5 CAPLUS
CN Piperazine, 1-ethyl-4-(5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



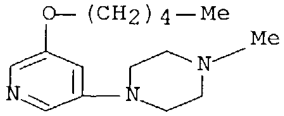
RN 303159-79-7 CAPLUS
CN Piperazine, 1-methyl-4-(5-propoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 303160-85-2 CAPLUS
CN Piperazine, 1-methyl-4-[5-(pentyloxy)-3-pyridinyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

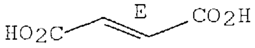
CRN 303160-84-1
CMF C15 H25 N3 O



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

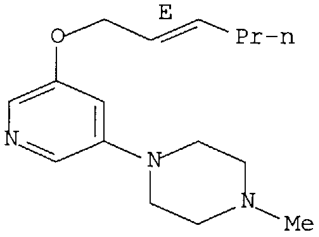


RN 303160-87-4 CAPLUS
CN Piperazine, 1-[5-[(2E)-2-hexenyloxy]-3-pyridinyl]-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 303160-86-3
CMF C16 H25 N3 O

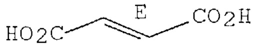
Double bond geometry as shown.



CM 2

CRN 110-17-8
CMF C4 H4 O4

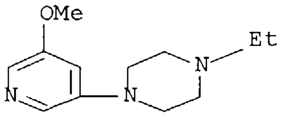
Double bond geometry as shown.



RN 303160-90-9 CAPLUS
CN Piperazine, 1-ethyl-4-(5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1)(9CI) (CA INDEX NAME)

CM 1

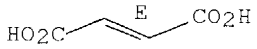
CRN 303159-77-5
CMF C12 H19 N3 O



CM 2

CRN 110-17-8
CMF C4 H4 O4

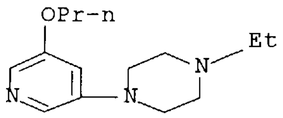
Double bond geometry as shown.



RN 303160-92-1 CAPLUS
CN Piperazine, 1-ethyl-4-(5-propoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

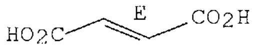
CRN 303160-91-0
CMF C14 H23 N3 O



CM 2

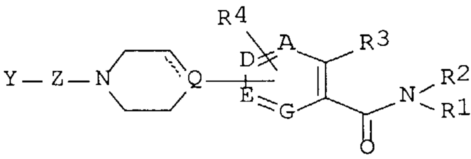
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

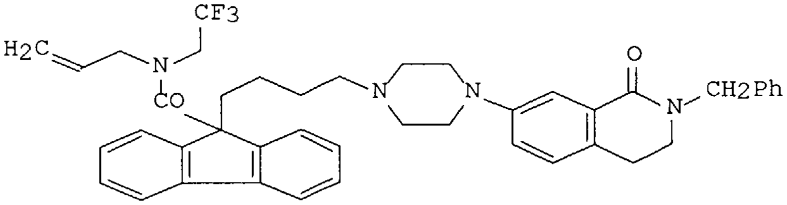


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 20 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:742072  CAPLUS Full-text
DN   133:309907
TI   Preparation of nitrogen-containing heterocyclic compounds and benzamide
     compounds as hypolipidemics and antiarteriosclerotics
IN   Ohkura, Naoto; Hiraiwa, Yukiko; Matsushima, Tetsuya; Sasaki, Kazue;
     Yamamoto, Takehiro; Shiotani, Masaharu; Suzuki, Shigeki; Nakatani,
Yuuko;
     Kuroda, Chizuko; Nagasawa, Mieko; Katano, Kiyoaki
PA   Meiji Seika Kaisha, Ltd., Japan
SO   PCT Int. Appl., 284 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2000061556      A1   20001019      WO 2000-JP2329   20000410
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
             CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2000036759      A5   20001114      AU 2000-36759    20000410
     BR 2000009650      A    20020102      BR 2000-9650     20000410
     EP 1180514         A1   20020220      EP 2000-915465   20000410
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
PRAI JP 1999-102559     A    19990409
     JP 1999-118490     A    19990426
     JP 1999-119043     A    19990427
     WO 2000-JP2329     W    20000410
OS   MARPAT 133:309907
GI
```



I



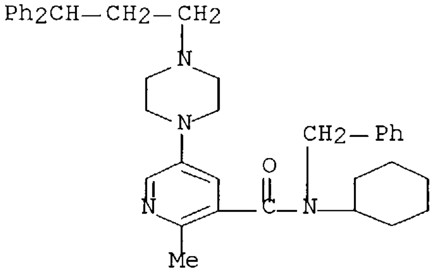
II

```
AB   The title compds. [I; R1 and R2 represent each (un)substituted C1-6
     alkyl or alkoxy, C3-8 cycloalkyl, Ph, C2-6 alkenyl or alkynyl, 5- or 6-
     membered ring (un)saturated heterocyclyl; R3 and R4 represent each
     hydrogen, (un)substituted C1-6 alkyl, halo, OH, cyano, C2-5
     alkoxycarbonyl, C1-6 alkoxy, or CO2H ; or R2 and R3 may be bonded to
```

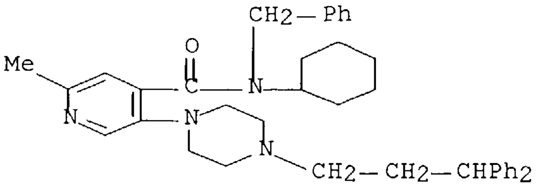
each other to form (CH2)m, N:CH, CH:N, or (C1-6 alkyl)-C:N; wherein m is 1 or 2; A, D, E and G represent each C, or one of A, D, E and G represents N and the remainders represent C; Q represents N or C; Y represents a group represented by general formula Q1 (wherein X represents hydrogen, CONR5R6, etc.; R8 represents nil or a bond, O, etc.; and R9 and R10 represent each hydrogen, alkyl, etc.); and Z represents (CH2)n, O(CH2)i, or CONH(CH2)i; wherein n is 0-6; i is 1-6] are prepared These compds. have an effect of inhibiting the biosynthesis of triglycerides in the liver and an effect of inhibiting the secretion of apolipoprotein B-containing lipoproteins from the liver (the latter effect being particularly excellent), without showing the side effect of fat accumulation in the liver, and are useful in treating and preventing hyperlipemia, arteriosclerotic diseases, and pancreatitis. Thus, to a solution of 2-benzyl-7-[4-[4-[9-(2,2,2-trifluoroethylcarbamoyl)-9H- fluoren-9-yl]butyl]piperazin-1-yl]-3,4-dihydro-2H-isoquinolin-1-one in PhMe were added NaOH, K2CO3, tetrabutylammonium hydrogen sulfate, and allyl bromide and the resulting mixture was stirred at 60° overnight to give title compound (II). II in vitro inhibited the secretion of apolipoprotein B by 89% and the biosynthesis of triglycerides by 89% in HepG2 cells. Tablet and capsule formulations were also described.

IT **301666-83-1P 301666-86-4P 301666-91-1P**
301666-95-5P 301666-96-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrogen-containing heterocyclic compds. and benzamide compds.
as hypolipidemics and antiarteriosclerotics and inhibitors of
apolipoprotein B-containing lipoproteins and biosynthesis of triglycerides)

RN 301666-83-1 CAPLUS
CN 3-Pyridinecarboxamide, N-cyclohexyl-5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

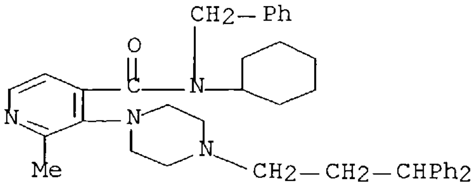


RN 301666-86-4 CAPLUS
CN 4-Pyridinecarboxamide, N-cyclohexyl-5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



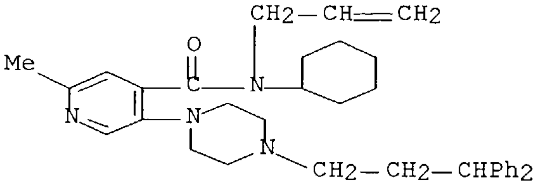
RN 301666-91-1 CAPLUS

CN 4-Pyridinecarboxamide, N-cyclohexyl-3-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



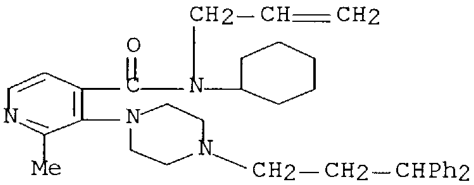
RN 301666-95-5 CAPLUS

CN 4-Pyridinecarboxamide, N-cyclohexyl-5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-N-2-propenyl- (9CI) (CA INDEX NAME)



RN 301666-96-6 CAPLUS

CN 4-Pyridinecarboxamide, N-cyclohexyl-3-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-N-2-propenyl- (9CI) (CA INDEX NAME)

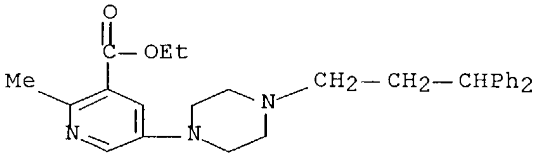


IT **301666-84-2P 301666-85-3P 301666-89-7P**
301666-90-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT(Reactant or reagent) (preparation of nitrogen-containing heterocyclic compds. and benzamide compds. as hypolipidemics and antiarteriosclerotics and inhibitors of apolipoprotein B-containing lipoproteins and biosynthesis of triglycerides)

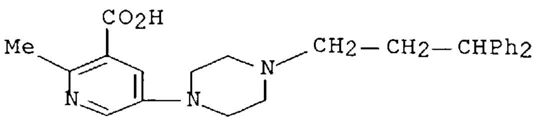
RN 301666-84-2 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)



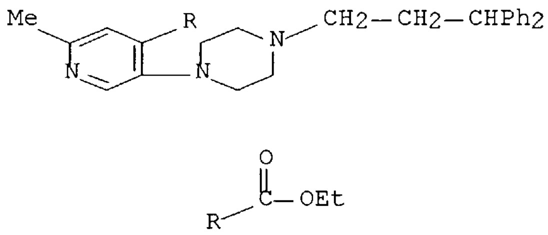
RN 301666-85-3 CAPLUS

CN 3-Pyridinecarboxylic acid, 5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl- (9CI) (CA INDEX NAME)



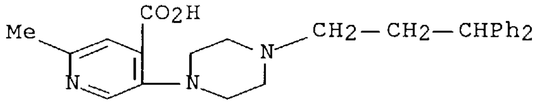
RN 301666-89-7 CAPLUS

CN 4-Pyridinecarboxylic acid, 5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl-, ethyl ester (9CI) (CA INDEX NAME)



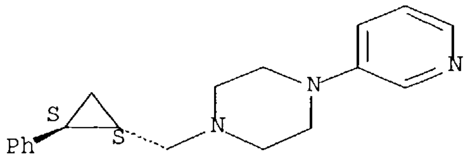
RN 301666-90-0 CAPLUS

CN 4-Pyridinecarboxylic acid, 5-[4-(3,3-diphenylpropyl)-1-piperazinyl]-2-methyl- (9CI) (CA INDEX NAME)



RE.CNT 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 21 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:688691  CAPLUS Full-text
DN   134:177
TI   trans-1-[(2-Phenylcyclopropyl)methyl]-4-arylpiperazines: mixed dopamine
     D2/D4 receptor antagonists as potential antipsychotic agents
AU   Zhang, Xiaoyan; Hodgetts, Kevin; Rachwal, Stanislaw; Zhao, He; Wasley,
Jan
     W. F.; Craven, Kimberly; Brodbeck, Robbin; Kieltyka, Andrzej; Hoffman,
     Diane; Bacolod, Maria D.; Girard, Brian; Tran, Jennifer; Thurkauf,
Andrew
CS   Neurogen Corporation, Branford, CT, 06405, USA
SO   Journal of Medicinal Chemistry (2000), 43(21), 3923-3932
     CODEN: JMCMAR; ISSN: 0022-2623
PB   American Chemical Society
DT   Journal
LA   English
AB    The dopaminergic receptor profile of a series of trans-1-[(2-
      phenylcyclopropyl)methyl]-4-arylpiperazines was examined  Aromatic
      substitution patterns were varied with the goal of identifying a
      compound having affinities for the D2 and D4 receptors in a ratio
      similar to that observed for the atypical neuroleptic clozapine.  The
      compds. (1S,2S)-trans-1-[(2- phenylcyclopropyl)methyl]-4-(2,4-
      dichlorophenyl)piperazine (5m) and (1S,2S)-trans-1-[(2-
      phenylcyclopropyl)methyl]-4-(2,4- dimethylphenyl)piperazine (5t) were
      selected for functional antagonists at D2 and D4 receptors and had a
      D2/D4 ratio approximating that of clozapine; they proved inactive in
      behavioral tests of antipsychotic activity.
IT   307952-07-4P
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
     study, unclassified); PRP (Properties); SPN (Synthetic preparation);
BIOL
     (Biological study); PREP (Preparation)
        (trans-1-[(2-phenylcyclopropyl)methyl]-4-arylpiperazines: mixed
        dopamine D2/D4 receptor antagonists as potential antipsychotic
agents)
RN   307952-07-4  CAPLUS
CN   Piperazine, 1-[[(1R,2R)-2-phenylcyclopropyl]methyl]-4-(3-pyridinyl)-,
     dihydrobromide, rel- (9CI)  (CA INDEX NAME)

Relative stereochemistry.
```



```
            ●2  HBr

RE.CNT  31     THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 22 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:573773  CAPLUS Full-text
DN   133:177025
TI   Preparation of arylacrylamides and related compounds as inhibitors of
     Factor Xa.
IN   Song, Yonghong; Zhu, Bing-yan; Scarborough, Robert M.; Clizbe, Lane;
Jia,
     Zhaozhong Jon; Su, Ting; Teng, Willy
PA   Cor Therapeutics Inc., USA
SO   PCT Int. Appl., 159 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   WO 2000047554      A2   20000817      WO 2000-US3405   20000211
     WO 2000047554      A3   20010809
        W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
           CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
           IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
           MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
           SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
           BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
           DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
           CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     EP 1159264         A2   20011205      EP 2000-917623   20000211
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
           IE, SI, LT, LV, FI, RO
     US 6399627         B1   20020604      US 2000-501371   20000211
     JP 2002536432      T2   20021029      JP 2000-598475   20000211
     US 6545054         B1   20030408      US 2000-501370   20000211
PRAI US 1999-119640P    P    19990211
     WO 2000-US3405     W    20000211
OS   MARPAT 133:177025
AB   ABDECG1:CG2KL [A = (substituted) Ph, naphthyl, (aromatic) heterocyclyl;
     B = bond, CO, NR3, CR3aR3b, CONR3, SO2, O, SO2NR, NR3SO2, etc.; R3, R3a,
     R3b = H, alkyl, alkenyl, alkynyl, cycloalkyl, alkylphenyl, etc.; D =
     (substituted) Ph, heteroaryl; E = bond, CO, CONR5, SO2NR5, CH2SO2, etc.;
     R5 = H, OH, alkoxy, alkyl, alkenyl, alkynyl, cycloalkyl, alkylphenyl,
     etc.; K = (substituted) Ph, naphthyl, mono- or bicyclic heterocyclyl; L
     = H, cyano, CONR12R13, (CH2)nNR12R13, etc.; n = 0-2; R12, R13 = H, OR14,
     NR14R15, alkyl, (substituted) alkylphenyl, alkylnaphthyl, etc.; R14, R15
     = H, alkyl, alkoxycarbonyl, CONH2, alkyl, etc.; G1, G2 = H, halo, alkyl,
     haloalkyl, cyano, NO2, alkenyl, alkynyl, cycloalkyl, cyanoalkyl, etc.],
     were prepared as inhibitors of Factor Xa (no data).  Thus, [[2-(4-
     aminophenyl)phenyl]sulfonyl]tert-butylamine (preparation given) in
     CH2Cl2 was treated with Me3Al in hexane and then with Me 3-(3-
     cyanophenyl)acrylate to give 19% N-[4-[(2-tert-
     butylaminosulfonyl)phenyl]phenyl]-3-(3-cyanophenyl)acrylamide.  The
     latter in MeOH was treated with HCl to give a residue which was refluxed
     with NH4OAc in MeOH to give 35% (2E)-N-[4-[(2-
     aminosulfonyl)phenyl]phenyl]-3-(3- amidinophenyl)-3-acrylamide.
IT   288308-77-0P
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
```

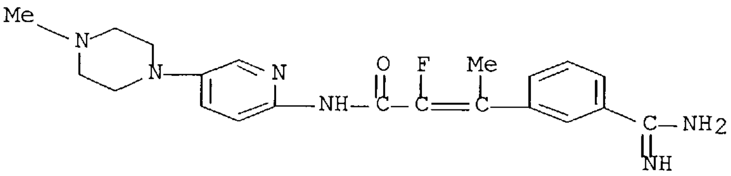
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)

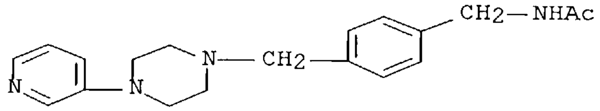
(preparation of arylacrylamides and related compds. as inhibitors of Factor Xa)

RN 288308-77-0 CAPLUS

CN 2-Butenamide, 3-[3-(aminoiminomethyl)phenyl]-2-fluoro-N-[5-(4-methyl-1-piperazinyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

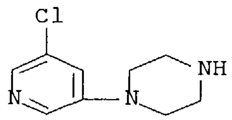


L23 ANSWER 23 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:380060 CAPLUS Full-text
DN 133:144477
TI Novel DMARDs on the basis of a new concept of dual cytokine regulation, TNF-α suppression and IL-10 augmentation
AU Hanano, Tokushi; Adachi, Kunitomo; Aoki, Yoshiyuki; Morimoto, Hiroshi; Naka, Yoichi; Hisadome, Masao; Fukuda, Tetsuko; Sumichika, Hiroshi
CS Drug Discovery Laboratories, Pharmaceutical Research Division, Yoshitomi Pharmaceutical Industries, Ltd., Iruma, 358-0026, Japan
SO Bioorganic & Medicinal Chemistry Letters (2000), 10(9), 881-884
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English
AB A series of arylpiperazine derivs. was synthesized to obtain agents showing apparent therapeutic effects in a chronic inflammatory animal model, starting from a lead possessing potent dual cytokine regulatory activity in vivo. We found a pyrimidylpiperazine derivative 17c showing the dual regulatory activity and an excellent therapeutic effect in an adjuvant-induced arthritis model.
IT **223512-02-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel DMARDs on the basis of a new concept of dual cytokine regulation)
RN 223512-02-5 CAPLUS
CN Acetamide, N-[[4-[[4-(3-pyridinyl)-1-piperazinyl]methyl]phenyl]methyl]- (9CI) (CA INDEX NAME)



RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

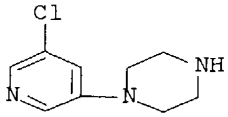
L23 ANSWER 24 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:293414 CAPLUS Full-text
DN 133:99064
TI Novel potent ligands for the central nicotinic acetylcholine receptor:
synthesis, receptor binding, and 3D-QSAR analysis
AU Nielsen, Simon Feldbk; Nielsen, Elsebet Ostergaard; Olsen, Gunnar M.;
Liljefors, Tommy; Peters, Dan
CS NeuroSearch A/S, Ballerup, DK-2750, Den.
SO Journal of Medicinal Chemistry (2000), 43(11), 2217-2226
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
AB In the past few years the focus on central acetylcholine receptors has shifted from compds. with affinity for muscarinic acetylcholine receptors (mAChR) to compds. with affinity for nicotinic acetylcholine receptors (nAChR). The therapeutic potential includes treatment of a variety of diseases, e.g., Alzheimer's disease, Parkinson's disease, and Tourette's syndrome. This work describes the synthesis of six novel series of potent ligands with nanomolar affinity for the α4β2 nAChR subtype. Structure-activity relationship (SAR) was evaluated by the calcn. of a 3D-QSAR model. 3D-QSAR anal. of the compds. using the GRID/GOLPE methodol. resulted in a model of high quality (R2 = 0.97, Q2 = 0.81). The coefficient plots reveal that the steric interactions between the target and our compds. are of major importance for the affinity. Bulky substituents in the 6-position of the pyridine ring will reduce the affinity of the compds., whereas bulky ring systems including a sp3-nitrogen will increase the affinity of the compds.
IT **223794-95-4P 223794-96-5P**, Piperazine,
1-(5-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) **223795-11-7P**
223795-12-8P
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
process); BSU (Biological study, unclassified); PRP (Properties); SPN
(Synthetic preparation); THU (Therapeutic use); BIOL (Biological study);
PREP (Preparation); PROC (Process); USES (Uses)
(synthesis, receptor binding, and 3D-QSAR anal. of novel potent ligands
for the central nAChR)
RN 223794-95-4 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223794-96-5 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)
(CA INDEX NAME)

CM 1

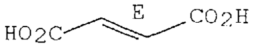
CRN 223794-95-4
CMF C9 H12 Cl N3



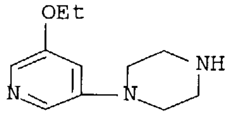
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



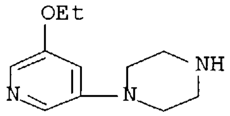
RN 223795-11-7 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223795-12-8 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

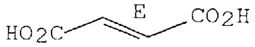
CM 1

CRN 223795-11-7
CMF C11 H17 N3 O



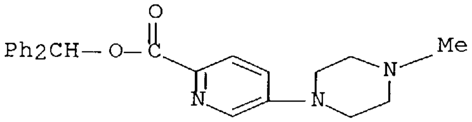
CM 2
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



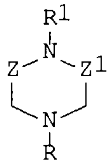
RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 25 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:646282 CAPLUS Full-text
DN 131:299355
TI A facile route to aryl amines. Nucleophilic substitution of aryl triflates
AU Schio, Laurent; Lemoine, Guy; Klich, Michel
CS Hoechst Marion Roussel, Romainville, F-93235, Fr.
SO Synlett (1999), (10), 1559-1562
CODEN: SYNLES; ISSN: 0936-5214
PB Georg Thieme Verlag
DT Journal
LA English
OS CASREACT 131:299355
AB The aromatic nucleophilic substitution (SNAr) between aryl triflates and secondary amines was studied. In the absence of solvent, the reaction proceeds at room temperature for nitro- and cyano-activated aryl triflates and requires higher temps. in the case of carboxy activation. Variable triflate reactivity could be explained in terms of frontier MO theory. This methodol. was applied for the synthesis of piperidylpyridines.
IT **247042-68-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of aryl amines by nucleophilic substitution of aryl triflates)
RN 247042-68-8 CAPLUS
CN 2-Pyridinecarboxylic acid, 5-(4-methyl-1-piperazinyl)-, diphenylmethyl ester (9CI) (CA INDEX NAME)



App's

```
L23  ANSWER 26 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:299480  CAPLUS Full-text
DN   130:325154
TI   Preparation of N-pyridylpiperazines and analogs as nicotinic receptor
     ligands
IN   Peters, Dan; Olsen, Gunnar M.; Nielsen, Simon Feldbaek; Nielsen, Elsebet
     Ostergaard
PA   Neurosearch A/S, Den.
SO   PCT Int. Appl., 68 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.   DATE
     ---------------    ----  --------      ---------------   --------
PI   WO 9921834          A1   19990506      WO 1998-DK465     19981027
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW,
             MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
             TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,
             TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2306093          AA   19990506      CA 1998-2306093   19981027
     AU 9897368          A1   19990517      AU 1998-97368     19981027
     AU 744539           B2   20020228
     ZA 9809771          A    19990929      ZA 1998-9771      19981027
     EP 1027336          A1   20000816      EP 1998-951286    19981027
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 9813279          A    20000822      BR 1998-13279     19981027
     TR 200001171        T2   20001023      TR 2000-20000117119981027
     EE 200000178        A    20010416      EE 2000-20000017819981027
     JP 2001521025       T2   20011106      JP 2000-517946    19981027
     NZ 503520           A    20020828      NZ 1998-503520    19981027
     RU 2205179          C2   20030527      RU 2000-110744    19981027
     CN 1131211          B    20031217      CN 1998-810601    19981027
     NO 2000002132       A    20000426      NO 2000-2132      20000426
     US 2004072823       A1   20040415      US 2003-677240    20031003
PRAI DK 1997-1225        A    19971027
     DK 1998-409         A    19980324
     DK 1998-796         A    19980619
     WO 1998-DK465       W    19981027
     US 2000-528176      A3   20000317
OS   MARPAT 130:325154
GI
```



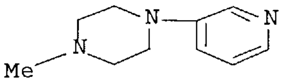
I

AB Title compds. [I; R = H, (cyclo)alkyl, aralkyl; R1 = C6H4R2 or (un)substituted heteroaryl; R2 = NH2, NO2, OH, alkoxy; Z = (CH2)0-2; Z1 = (CH2)1-3] were prepared Thus, 1-tert-butoxycarbonylpiperazine was N-arylated by 3-bromopyridine and the deprotected product N-methylated to give I (R = Me, R1 = 3-pyridyl, Z = Z1 = CH2). Data for biol activity of I were given.

IT **223794-26-1P 223794-27-2P 223794-36-3P**
223794-47-6P 223794-48-7P 223794-52-3P
223794-53-4P 223794-57-8P 223794-58-9P
223794-62-5P 223794-63-6P 223794-69-2P
223794-73-8P 223794-74-9P 223794-93-2P
223794-94-3P 223794-95-4P 223794-96-5P
223794-97-6P 223794-98-7P 223795-11-7P
223795-12-8P 223795-15-1P 223795-16-2P
223795-19-5P 223795-21-9P 223795-22-0P
223795-40-2P 223795-41-3P 223797-34-0P
223797-37-3P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-pyridylpiperazines and analogs as nicotinic receptor ligands)

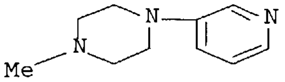
RN 223794-26-1 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223794-27-2 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

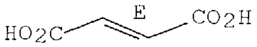
CRN 223794-26-1
CMF C10 H15 N3



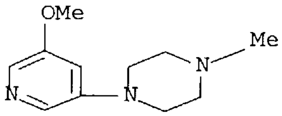
CM 2

CRN 110-17-8
CMF $C_4 H_4 O_4$

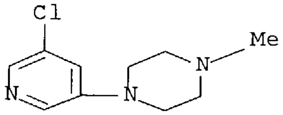
Double bond geometry as shown.



RN 223794-36-3 CAPLUS
CN Piperazine, 1-(5-methoxy-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



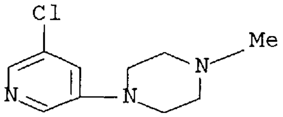
RN 223794-47-6 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 223794-48-7 CAPLUS
CN Piperazine, 1-(5-chloro-3-pyridinyl)-4-methyl-, (2E)-2-butenedioate (1:1)
(9CI) (CA INDEX NAME)

CM 1

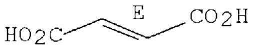
CRN 223794-47-6
CMF $C_{10} H_{14} Cl N_3$



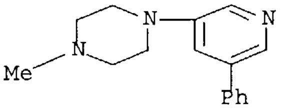
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



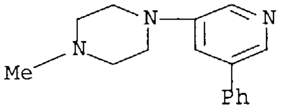
RN 223794-52-3 CAPLUS
CN Piperazine, 1-methyl-4-(5-phenyl-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223794-53-4 CAPLUS
CN Piperazine, 1-methyl-4-(5-phenyl-3-pyridinyl)-, (2E)-2-butenedioate
(1:1)
(9CI) (CA INDEX NAME)

CM 1

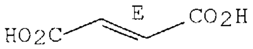
CRN 223794-52-3
CMF C16 H19 N3



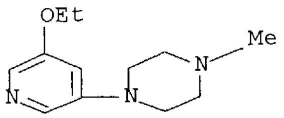
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



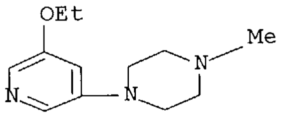
RN 223794-57-8 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 223794-58-9 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-methyl-, (2E)-2-butenedioate (1:1)
(9CI) (CA INDEX NAME)

CM 1

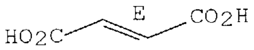
CRN 223794-57-8
CMF C12 H19 N3 O



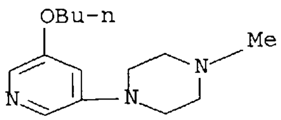
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



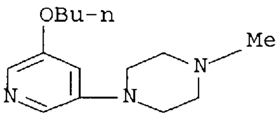
RN 223794-62-5 CAPLUS
CN Piperazine, 1-(5-butoxy-3-pyridinyl)-4-methyl- (9CI) (CA INDEX NAME)



RN 223794-63-6 CAPLUS
CN Piperazine, 1-(5-butoxy-3-pyridinyl)-4-methyl-, (2E)-2-butenedioate (1:1)
(9CI) (CA INDEX NAME)

CM 1

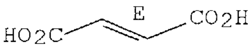
CRN 223794-62-5
CMF C14 H23 N3 O



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

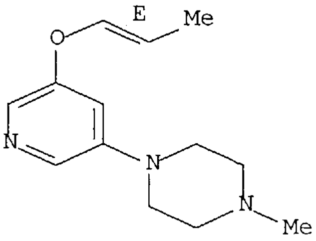


RN 223794-69-2 CAPLUS
CN Piperazine, 1-methyl-4-[5-[(1E)-1-propenyloxy]-3-pyridinyl]-,
(2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 223794-68-1
CMF C13 H19 N3 O

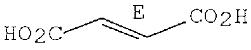
Double bond geometry as shown.



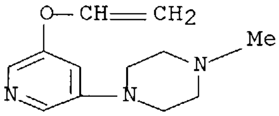
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



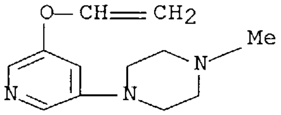
RN 223794-73-8 CAPLUS
CN Piperazine, 1-[5-(ethenyloxy)-3-pyridinyl]-4-methyl- (9CI) (CA INDEX NAME)



RN 223794-74-9 CAPLUS
CN Piperazine, 1-[5-(ethenyloxy)-3-pyridinyl]-4-methyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

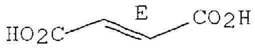
CRN 223794-73-8
CMF C12 H17 N3 O



CM 2

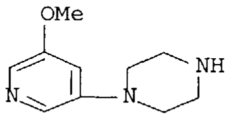
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 223794-93-2 CAPLUS

CN Piperazine, 1-(5-methoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)

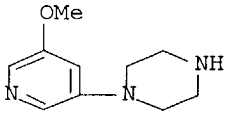


RN 223794-94-3 CAPLUS

CN Piperazine, 1-(5-methoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

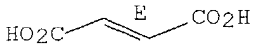
CRN 223794-93-2
CMF C10 H15 N3 O



CM 2

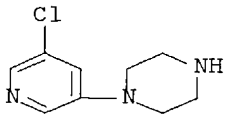
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 223794-95-4 CAPLUS

CN Piperazine, 1-(5-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



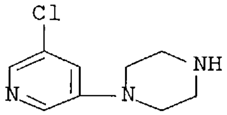
RN 223794-96-5 CAPLUS

CN Piperazine, 1-(5-chloro-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 223794-95-4

CMF C9 H12 Cl N3

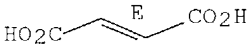


CM 2

CRN 110-17-8

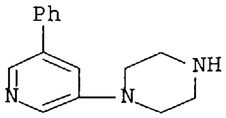
CMF C4 H4 O4

Double bond geometry as shown.



RN 223794-97-6 CAPLUS

CN Piperazine, 1-(5-phenyl-3-pyridinyl)- (9CI) (CA INDEX NAME)

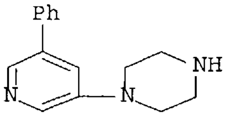


RN 223794-98-7 CAPLUS

CN Piperazine, 1-(5-phenyl-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

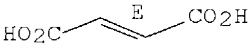
CRN 223794-97-6
CMF C15 H17 N3



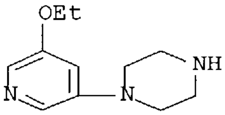
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



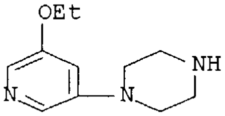
RN 223795-11-7 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223795-12-8 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

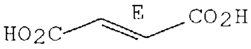
CRN 223795-11-7
CMF C11 H17 N3 O



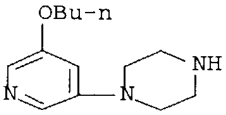
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



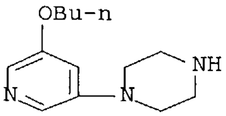
RN 223795-15-1 CAPLUS
CN Piperazine, 1-(5-butoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



RN 223795-16-2 CAPLUS
CN Piperazine, 1-(5-butoxy-3-pyridinyl)-, (2E)-2-butenedioate (1:1) (9CI)
(CA INDEX NAME)

CM 1

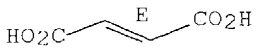
CRN 223795-15-1
CMF C13 H21 N3 O



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

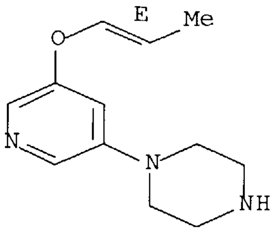


RN   223795-19-5   CAPLUS
CN   Piperazine, 1-[5-[(1E)-1-propenyloxy]-3-pyridinyl]-, (2E)-2-butenedioate
      (1:1) (9CI)   (CA INDEX NAME)

CM   1

CRN   223795-18-4
CMF   C12 H17 N3 O

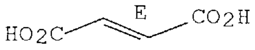
Double bond geometry as shown.



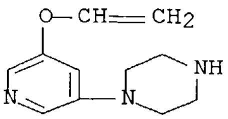
CM   2

CRN   110-17-8
CMF   C4 H4 O4

Double bond geometry as shown.



RN   223795-21-9   CAPLUS
CN   Piperazine, 1-[5-(ethenyloxy)-3-pyridinyl]- (9CI)   (CA INDEX NAME)

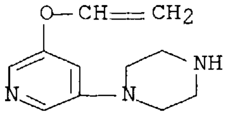


RN   223795-22-0   CAPLUS

CN Piperazine, 1-[5-(ethenyloxy)-3-pyridinyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

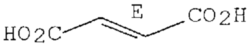
CRN 223795-21-9
CMF C11 H15 N3 O



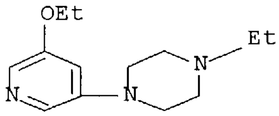
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



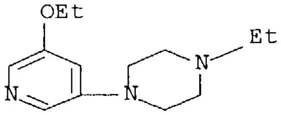
RN 223795-40-2 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-ethyl- (9CI) (CA INDEX NAME)



RN 223795-41-3 CAPLUS
CN Piperazine, 1-(5-ethoxy-3-pyridinyl)-4-ethyl-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

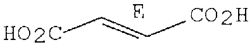
CRN 223795-40-2
CMF C13 H21 N3 O



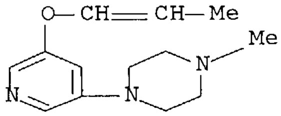
CM 2

CRN 110-17-8
CMF C4 H4 O4

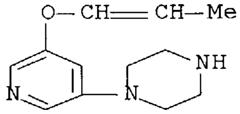
Double bond geometry as shown.



RN 223797-34-0 CAPLUS
CN Piperazine, 1-methyl-4-[5-(1-propenyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

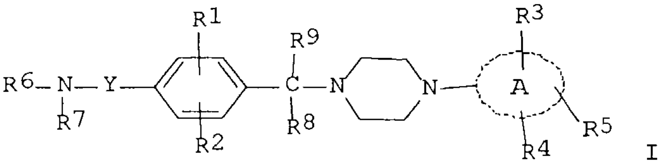


RN 223797-37-3 CAPLUS
CN Piperazine, 1-[5-(1-propenyloxy)-3-pyridinyl]- (9CI) (CA INDEX NAME)

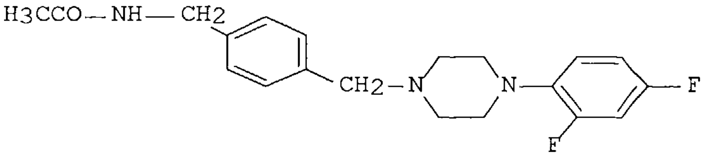


RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 27 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:271336  CAPLUS Full-text
DN   130:311814
TI   Preparation of piperazine derivatives as TNF production inhibitors and
     IL-10 production promoters
IN   Adachi, Kunitomo; Aoki, Yoshiyuki; Hanano, Tokushi; Morimoto, Hiroshi;
     Hisadome, Masao
PA   Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO   PCT Int. Appl., 304 pp.
     CODEN: PIXXD2
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
PI   WO 9919301         A1   19990422       WO 1998-JP4613   19981013
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE,
             KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2306811         AA   19990422       CA 1998-2306811  19981013
     AU 9894604         A1   19990503       AU 1998-94604    19981013
     AU 744577          B2   20020228
     EP 1029851         A1   20000823       EP 1998-947846   19981013
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     BR 9814820         A    20001003       BR 1998-14820    19981013
     NZ 504465          A    20011130       NZ 1998-504465   19981013
     JP 3329337         B2   20020930       JP 2000-515874   19981013
     RU 2199534         C2   20030227       RU 2000-112020   19981013
     US 6455528         B1   20020924       US 2000-529491   20000414
     US 2003055064      A1   20030320       US 2002-187286   20020702
     US 2003018034      A1   20030123       US 2002-209228   20020801
PRAI JP 1997-280880     A    19971014
     JP 1998-261100     A    19980916
     WO 1998-JP4613     W    19981013
     US 2000-529491     A3   20000414
OS   MARPAT 130:311814
GI
```



I



II

AB The title compds. I [R1 and R2 represent each hydrogen, halogeno, lower alkyl, lower alkoxy, optionally substituted amino, nitro, hydroxy or cyano; R3, R4 and R5 represent each hydrogen, halogeno, lower alkyl, lower alkoxy, nitro, optionally substituted amino or hydroxy; R6 and R7 represent each hydrogen, optionally halogenated lower alkyl, aralkyl, acyl or halogenated lower acyl; R8 and R9 represent each hydrogen or lower alkyl; Y represents lower alkylene, etc.; and the ring A represents Ph, pyrimidyl, thiazolyl, pyridyl, pyrazyl or imidazolyl] are prepared I are useful as preventives or remedies for, e.g., chronic inflammatory diseases, acute inflammatory diseases, inflammatory diseases caused by infection, autoimmune diseases, allergic diseases and other TNF-α-mediated diseases. The title compound II inhibited TNF production in mice; at 30 mg/kg orally, II clearly inhibited adjuvant arthritis in rats.

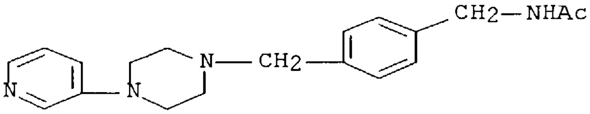
IT **223512-02-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperazine derivs. as TNF production inhibitors and IL-10 production promoters)

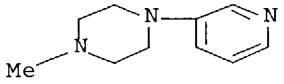
RN 223512-02-5 CAPLUS

CN Acetamide, N-[[4-[[4-(3-pyridinyl)-1-piperazinyl]methyl]phenyl]methyl]- (9CI) (CA INDEX NAME)

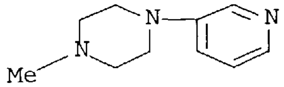


RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 28 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:235769 CAPLUS Full-text
DN 130:338083
TI Hybridized and isosteric analogs of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) with central nicotinic action
AU Manetti, Dina; Bartolini, Alessandro; Borea, Pier Andrea; Bellucci, Cristina; Dei, Silvia; Ghelardini, Carla; Gualtieri, Fulvio; Romanelli, Maria Novella; Scapecchi, Serena; Teodori, Elisabetta; Varani, Katia
CS Dipartimento di Scienze Farmaceutiche, Universita di Firenze, Florence, 50121, Italy
SO Bioorganic & Medicinal Chemistry (1999), 7(3), 457-465
CODEN: BMECEP; ISSN: 0968-0896
PB Elsevier Science Ltd.
DT Journal
LA English
AB A series of piperazine derivs., obtained by hybridization of N1-acetyl-N4-dimethylpiperazinium iodide (ADMP) and N1-phenyl-N4-dimethylpiperazinium iodide (DMPP) or of the corresponding tertiary bases with arecoline and arecolone or by isosteric substitution of the Ph ring of DMPP, has been synthesized. Hybridization afforded compds. that, both as tertiary bases and as iodomethylates, have no affinity for the nicotinic receptor. On the contrary, isosteric substitution gave compds. that maintain affinity for the receptor; among them, 1-methyl-4-(3- or 4-pyridinyl)piperazine show affinity in the nanomolar range for the nicotinic receptor. The pharmacol. profile of these isomeric compds. is quite interesting as they present differences in their peripheral and central effects, suggesting that they interact with different subtypes of the nicotinic receptor.
IT **223794-26-1P 224189-23-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central nicotinic action)
RN 223794-26-1 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



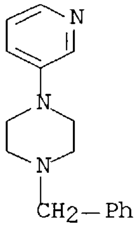
RN 224189-23-5 CAPLUS
CN Piperazine, 1-methyl-4-(3-pyridinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

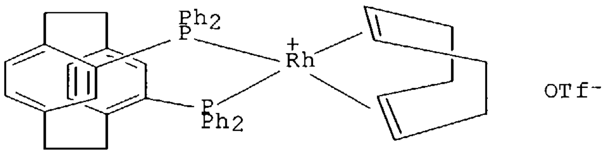
IT **13480-30-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (hybridized and isosteric analogs of N1-acetyl- and N1-phenyl-N4-dimethylpiperazinium iodide with central

```
     nicotinic action)
RN   13480-30-3  CAPLUS
CN   Piperazine, 1-(phenylmethyl)-4-(3-pyridinyl)-  (9CI)   (CA INDEX NAME)
```



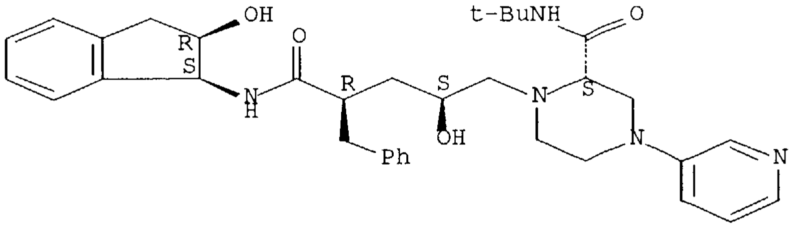
```
RE.CNT  47      THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 29 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1999:130430  CAPLUS Full-text
DN   130:196761
TI   Chiral bisphosphines
IN   Pye, Philip; Rossen, Kai; Volante, Ralph P.
PA   Merck and Co., Inc., USA
SO   U.S., 30 pp.
     CODEN: USXXAM
DT   Patent
LA   English
FAN.CNT 2
     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
PI   US 5874629         A    19990223      US 1997-866665   19970609
     US 6043387         A    20000328      US 1999-243859   19990203
PRAI US 1996-19590P     P    19960612
     US 1997-866665     A3   19970609
OS   MARPAT 130:196761
GI
```



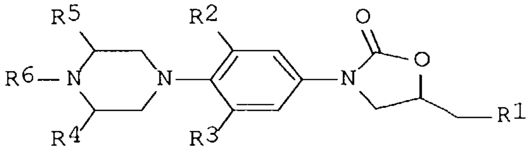
I

```
AB    New chiral bisphosphines are useful as key components in catalysts for
      asym. reactions, providing desirably high enantiomeric excess (ee).
      E.g., complex I was prepared and used as catalyst for the asym.
      hydrogenation of cinnamates, acrylates and keto esters.
IT   220750-14-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of chiral bisphosphines as stereoselective catalysts for
asym.
        reactions)
RN   220750-14-1  CAPLUS
CN   D-erythro-Pentonamide, 2,3,5-trideoxy-N-[(1S,2R)-2,3-dihydro-2-hydroxy-
1H-
     inden-1-yl]-5-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]-4-(3-
pyridinyl)-
     1-piperazinyl]-2-(phenylmethyl)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
```

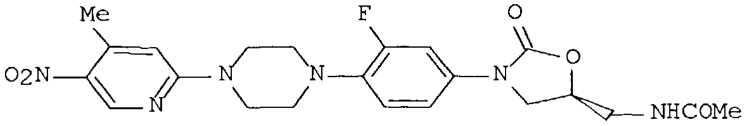


```
RE.CNT  4       THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
                ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

```
L23  ANSWER 30 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1998:65907  CAPLUS Full-text
DN   128:140728
TI   Preparation of pyridyl-piperazinyl-phenyl-oxazolidinones as
antibacterials
IN   Betts, Michael John; Darbyshire, Catherine Jane
PA   Zeneca Ltd., UK; Betts, Michael John; Darbyshire, Catherine Jane
SO   PCT Int. Appl., 63 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   WO 9801447         A1   19980115      WO 1997-GB1769    19970701
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
             UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,
             GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,
             GN, ML, MR, NE, SN, TD, TG
     AU 9733521         A1   19980202      AU 1997-33521     19970701
     EP 918770          A1   19990602      EP 1997-929405    19970701
         R:  CH, DE, FR, GB, IT, LI
     JP 2000514084      T2   20001024      JP 1998-504901    19970701
     ZA 9705951         A    19980106      ZA 1997-5951      19970703
PRAI GB 1996-14236      A    19960706
     WO 1997-GB1769     W    19970701
OS   MARPAT 128:140728
GI
```



I



II

AB   The title compds. [I; R1 = OH, Cl, F, etc.; R2, R3 = H, F; R4, R5 = H, Me; R6 = (un)substituted pyridyl linked via a ring carbon] and their pharmaceutically-acceptable salts, suitable N-oxides and in vivo hydrolysable esters, useful as antibacterial agents, were prepared and formulated. Thus, reaction of N-[(5S)-3-(3-fluoro-4-(piperazin-1-yl)phenyl)-2-oxooxazolidin-5-ylmethyl]acetamide trifluoroacetate salt with 4-chloropyridine hydrochloride in the presence of Et3N in H2O afforded the title compound (5S)-II which showed, e.g., MIC of 1.0 μg/mL against Staphylococcus aureus (Oxford).

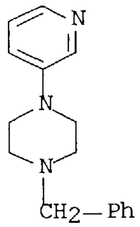
IT **13480-30-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridyl-piperazinyl-phenyl-oxazolidinones as antibacterials)

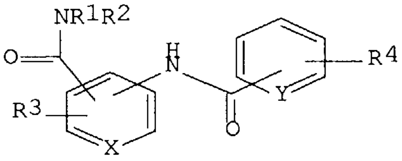
RN 13480-30-3 CAPLUS

CN Piperazine, 1-(phenylmethyl)-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)

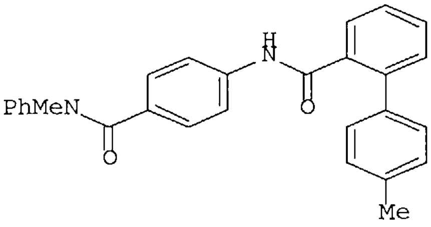


RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

```
L23  ANSWER 31 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1996:708296  CAPLUS Full-text
DN   125:328306
TI   Preparation of benzamide derivatives as vasopressin antagonists
IN   Setoi, Hiroyuki; Ohkawa, Takehiko; Zenkoh, Tatsuya; Hemmi, Keiji;
Tanaka,
     Hirokazu
PA   Fujisawa Pharmaceutical Co., Ltd., Japan
SO   PCT Int. Appl., 281 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   WO 9529152         A1   19951102      WO 1995-JP788     19950421
         W:  AU, CA, CN, JP, KR, MX, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     AU 9522674         A1   19951116      AU 1995-22674     19950421
     EP 757670          A1   19970212      EP 1995-916028    19950421
     EP 757670          B1   19990113
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     JP 09512528        T2   19971216      JP 1995-527525    19950421
     AT 175661          E    19990115      AT 1995-916028    19950421
     ES 2127524         T3   19990416      ES 1995-916028    19950421
     US 6211242         B1   20010403      US 1998-722243    19980130
PRAI GB 1994-8185       A    19940425
     WO 1995-JP788      W    19950421
OS   MARPAT 125:328306
GI
```



I



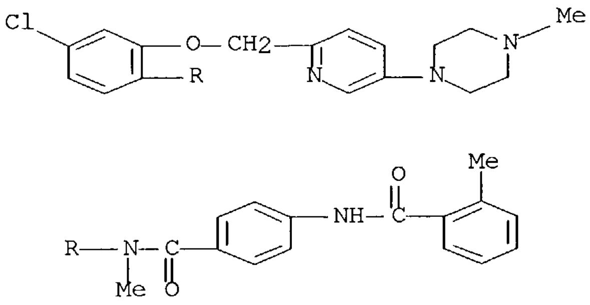
II

```
AB   Title compds. [I; (cyclo)alkyl, aryl, heterocyclyl, etc.; R2 =
     (cyclo)alkyl, arylalkyl, etc.; R3 = H, halo, alkyl, alkoxy, etc.; R4 =
     alkyl, (un)substituted aryl; X,Y = CH or N] were prepared  Thus, PhNHMe
     was amidated by 4-(O2N)C6H4COCl and the reduced product amidated by 4-
     MeC6H4C6H4(CO2H)-2 to give title compound II.  Data for in vitro
     vasopressin antagonism by I were given.
IT   183494-13-5P 183494-42-0P
     RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
```

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of benzamide derivs. as vasopressin antagonists)

RN 183494-13-5 CAPLUS

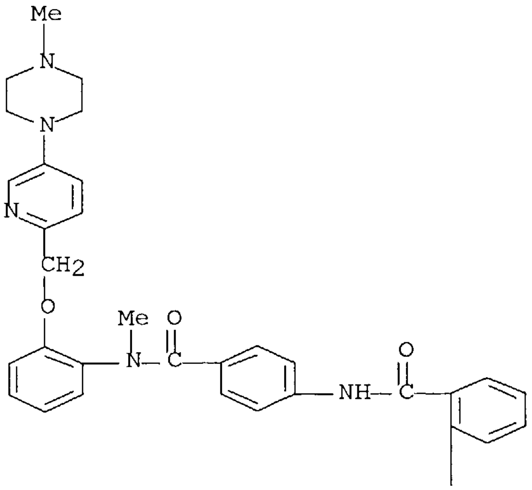
CN Benzamide, N-[4-chloro-2-[[5-(4-methyl-1-piperazinyl)-2-pyridinyl]methoxy]phenyl]-N-methyl-4-[(2-methylbenzoyl)amino]- (9CI) (CA INDEX NAME)



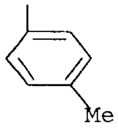
RN 183494-42-0 CAPLUS

CN [1,1'-Biphenyl]-2-carboxamide, 4'-methyl-N-[4-[[methyl[2-[[5-(4-methyl-1-piperazinyl)-2-pyridinyl]methoxy]phenyl]amino]carbonyl]phenyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

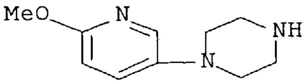


PAGE 2-A

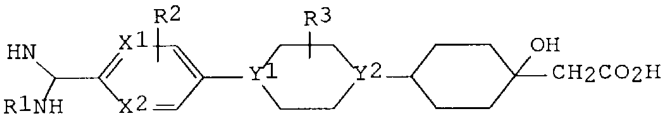


```
L23  ANSWER 32 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1994:638421  CAPLUS Full-text
DN   121:238421
TI   Pharmaceutical compositions containing substituted azolone derivatives
for
     treating diseases caused by helicobacter
IN   Heeres, Jan; Mostmans, Joseph Hector; Van Der Eycken, Luc Alfons Leo;
     Odds, Frank Christopher; Stokbroekx, Raymond Antoine; Van Der Aa, Marcel
     Jozef Maria
PA   Janssen Pharmaceutica N.V., Belg.
SO   PCT Int. Appl., 40 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 9418978          A1   19940901      WO 1994-EP380    19940209
         W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, LK, LV, MG,
             MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
             BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
     CA 2155830          AA   19940901      CA 1994-2155830  19940209
     AU 9461081          A1   19940914      AU 1994-61081    19940209
     AU 675508           B2   19970206
     EP 684821           A1   19951206      EP 1994-907534   19940209
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE
     CN 1118138          A    19960306      CN 1994-191221   19940209
     JP 08506821         T2   19960723      JP 1994-518613   19940209
     HU 73662            A2   19960930      HU 1995-1923     19940209
     PL 174836           B1   19980930      PL 1994-310348   19940209
     RU 2128659          C1   19990410      RU 1995-122796   19940209
     LT 3214             B    19950425      LT 1994-1874     19940218
     ZA 9401137          A    19950818      ZA 1994-1137     19940218
     IL 108703           A1   19980104      IL 1994-108703   19940218
     US 5650411          A    19970722      US 1995-491960   19950718
     FI 9503899          A    19950818      FI 1995-3899     19950818
     NO 9503254          A    19950911      NO 1995-3254     19950818
PRAI EP 1993-200474      A    19930219
     WO 1994-EP380       W    19940209
OS   MARPAT 121:238421
AB   Pharmaceutical compns. containing substituted azolone derivs. (Markush
     structure given) are used for for treating diseases caused by
     helicobacter.  A solution of 2-(chlorodimthylsilyl)-2-methylpropane in
     CH2Cl2 was added to a stirred solution of 2-[1-(4-bromobenzoyl)ethyl]-
     2,4-dihydro-4- [4-[4-(4-hydroxyphenyl)-1-piperazinyl]phenyl]-3H-1,2,4-
     triazol-3-one in pyridine under N atmospheric and stirred for 1 wk, then
     the mixture was evaporated and the residue was purified to obtain 2-[1-
     (4-bromobenzoyl)ethyl]-4-[4-[4-[4- [[(1,1,-
     dimethylethyl)dimethylsilyl]oxy]phenyl]-1-piperazinyl]phenyl]-2,4-
     dihydro-3H-1,2,4-triazol-3-one (I).  The MIC of I against Helicobacter
     pylori was 1 µM.  A capsule containing I 20 mg. was prepared
IT   158399-76-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
     RACT (Reactant or reagent)(pharmaceutical compns. containing substituted
     azolone derivs. for treating diseases caused by helicobacter)
RN   158399-76-9  CAPLUS
```

CN   Piperazine, 1-(6-methoxy-3-pyridinyl)- (9CI)   (CA INDEX NAME)



```
L23  ANSWER 33 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1993:603426  CAPLUS Full-text
DN   119:203426
TI   Cyclohexaneacetic acid derivatives as inhibitors of fibrinogen-dependent
     blood platelet aggregation
IN   Porter, Barry; Eldred, Colin David; Kelly, Henry Anderson
PA   Glaxo Group Ltd., UK
SO   Eur. Pat. Appl., 25 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   EP 537980          A1   19930421      EP 1992-309308    19921013
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,
SE
     WO 9308181         A1   19930429      WO 1992-EP2340    19921012
         W:  AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP,
             KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, UA, US
         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF,
             BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG
     AU 9226892         A1   19930521      AU 1992-26892     19921012
     EP 609282          A1   19940810      EP 1992-921322    19921012
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE
     JP 07500327        T2   19950112      JP 1992-507408    19921012
     CN 1073433         A    19930623      CN 1992-113088    19921015
     ZA 9207955         A    19930813      ZA 1992-7955      19921015
PRAI GB 1991-22016           19911016
     WO 1992-EP2340          19921012
OS   MARPAT 119:203426
GI
```



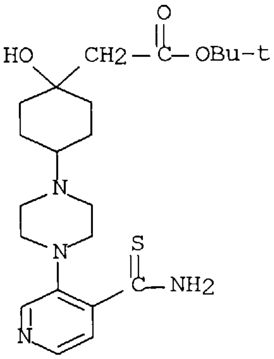
I

```
AB   Cyclohexaneacetic acid derivs. I (X1, X2, Y1 = CH, N, Y2 = N; Y1 = N, Y2
     = CH; R1 = H, OH, alkyl, CH2CF3, R2 = H; X1 = X2 = CH, R2 = F, Cl, Br,
     Ph, alkyl, R3 = H; Y1 = Y2 = N, R3 = alkyl, CH2OH) and salts and
     solvates thereof were prepared as inhibitors of fibrinogen-dependent,
     blood platelet aggregation.
IT   150506-44-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
     (Reactant or reagent)
        (preparation and acid-catalyzed hydrolysis of)
RN   150506-44-8  CAPLUS
CN   Cyclohexaneacetic acid, 4-[4-[4-(aminothioxomethyl)-3-pyridinyl]-1-
     piperazinyl]-1-hydroxy-, 1,1-dimethylethyl ester, mono(trifluoroacetate)
```

(salt) (9CI) (CA INDEX NAME)

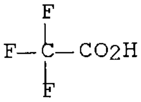
CM 1

CRN 150506-43-7
CMF C22 H34 N4 O3 S



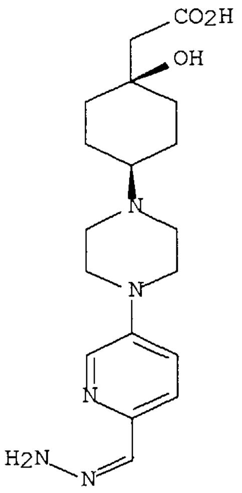
CM 2

CRN 76-05-1
CMF C2 H F3 O2



IT **150506-56-2P 150506-57-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and inhibition by, of fibrinogen-dependent blood platelet aggregation)
RN 150506-56-2 CAPLUS
CN Cyclohexaneacetic acid, 4-[4-[6-(hydrazonomethyl)-3-pyridinyl]-1-piperazinyl]-1-hydroxy-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.



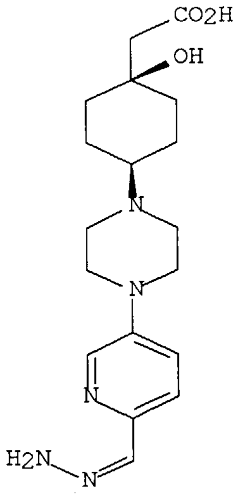
RN 150506-57-3 CAPLUS

CN Cyclohexaneacetic acid, 4-[4-[6-(hydrazonomethyl)-3-pyridinyl]-1-piperazinyl]-1-hydroxy-, cis-, trifluoroacetate (2:5) (salt) (9CI) (CA INDEX NAME)

CM 1

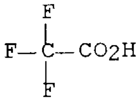
CRN 150506-56-2
CMF C18 H27 N5 O3

Relative stereochemistry.
Double bond geometry unknown.

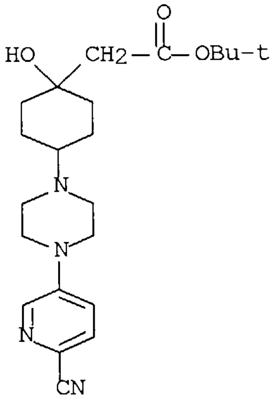


CM 2

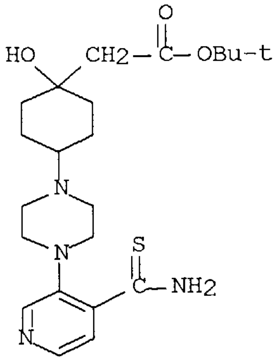
CRN 76-05-1
CMF C2 H F3 O2


$\mathrm{F-\overset{F}{\underset{F}{C}}-CO_2H}$

IT **150506-42-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(preparation and sulfurization of, with hydrogen sulfide)
RN 150506-42-6 CAPLUS
CN Cyclohexaneacetic acid, 4-[4-(6-cyano-3-pyridinyl)-1-piperazinyl]-1-hydroxy-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



IT **150506-43-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(preparation, S-alkylation, and ammonolysis of)
RN 150506-43-7 CAPLUS
CN Cyclohexaneacetic acid, 4-[4-[4-(aminothioxomethyl)-3-pyridinyl]-1-piperazinyl]-1-hydroxy-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

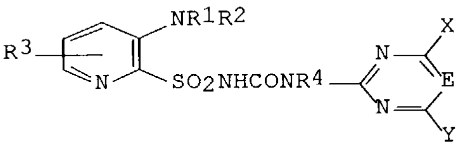


HO
CH2
O
C
OBu-t
N
N
S
C
NH2
N

L23 ANSWER 34 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:83702 CAPLUS Full-text
DN 116:83702
TI Preparation of N-pyridinylsulfonyl-N'-pyrimidinyl- and -triazinylureas as
herbicides and plant growth inhibitors
IN Foery, Werner; Schurter, Rolf
PA Ciba-Geigy A.-G., Switz.
SO Eur. Pat. Appl., 29 pp.
CODEN: EPXXDW
DT Patent
LA German
FAN.CNT 1

```
     PATENT NO.          KIND  DATE          APPLICATION NO.   DATE
     ---------------     ----  --------      ---------------   --------
PI   EP 459949            A1   19911204      EP 1991-810387    19910522
     EP 459949            B1   19960103
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     ES 2082175           T3   19960316      ES 1991-810387    19910522
     US 5221315           A    19930622      US 1991-705459    19910524
     CA 2043376           AA   19911201      CA 1991-2043376   19910528
     JP 04235984          A2   19920825      JP 1991-152571    19910528
     AU 9178046           A1   19911205      AU 1991-78046     19910529
     AU 647791            B2   19940331
     ZA 9104067           A    19920226      ZA 1991-4067      19910529
     US 5336773           A    19940809      US 1993-43231     19930406
PRAI CH 1990-1826              19900530
     US 1991-705459            19910524
```

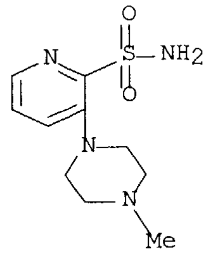
OS MARPAT 116:83702
GI



I

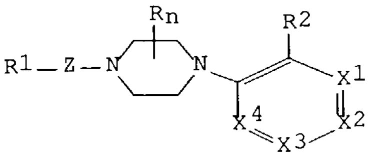
AB Title compds. I [R1, R2 = H, (substituted) C1-8 alkyl, (substituted) C3-8 cycloalkyl or NR1R2 = (substituted) 5-6 membered heterocyclyl which may be interrupted by O, S or NR7; R3 = H, halo, (substituted) C1-4 alkyl, C1-4 alkoxy, or C1-4 alkylthio; R4-R7 = H, C1-4 alkyl; X = (halo) C1-3 alkyl or C1-3 alkoxy; Y = (halo) C1-4 alkyl, C1-3 alkoxy, cyclopropyl, MeNH, Me2N; E = N, CH] were prepared Thus, n-butylamine was added to a mixture of 3-fluoro-2-pyridinylsulfonamide in THF and the mixture was stirred 18 h at 60° to give 3-(butylamino)-2-pyridinylsulfonamide. This was condensed with Ph N-(4,6-dimethoxy-2-pyrimidinyl)carbamate in the presence of a base to give title compound I (R1 = Bu; R2-R4 = H; X = Y = OMe; E = CH) (II). II at 70.8 ppm pre-emergent gave complete control of Nasturtium officinalis and Agrostis tenuis. Formulations of I were prepared

IT **138845-81-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for herbicides and plant growth inhibitors)
RN 138845-81-5 CAPLUS
CN 2-Pyridinesulfonamide, 3-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

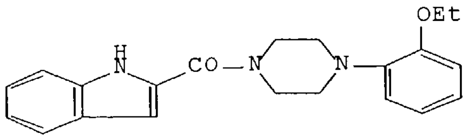


N
O
S
NH2
O
N
N
Me

```
L23  ANSWER 35 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1992:21074  CAPLUS Full-text
DN   116:21074
TI   Diaromatic substituted anti-AIDS compounds
IN   Romero, Donna Lee; Mitchell, Mark Allen; Thomas, Richard Charles;
Palmer,
     John Raymond; Tarpley, William Gary; Aristoff, Paul Adrian; Smith,
Herman
     W.
PA   Upjohn Co., USA
SO   PCT Int. Appl., 165 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.        KIND  DATE          APPLICATION NO.   DATE
     ---------------   ----  --------      ---------------   --------
PI   WO 9109849         A1   19910711      WO 1990-US7390    19901224
         W:  AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, RO,
             SD, SU, US
         RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT,
             LU, ML, MR, NL, SE, SN, TD, TG
     CA 2071529         AA   19910629      CA 1990-2071529   19901224
     CA 2071529         C    20010320
     AU 9171732         A1   19910724      AU 1991-71732     19901224
     AU 654808          B2   19941124
     EP 507861          A1   19921014      EP 1991-902628    19901224
     EP 507861          B1   19960911
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
     HU 61296           A2   19921228      HU 1992-2131      19901224
     JP 05503929        T2   19930624      JP 1991-502810    19901224
     JP 07110852        B4   19951129      JP 1990-502810    19901224
     AT 142621          E    19960915      AT 1991-902628    19901224
     ES 2093090         T3   19961216      ES 1991-902628    19901224
     RU 2099335         C1   19971220      RU 1992-5011431   19920131
     LV 10264           B    19951020      LV 1993-292       19930505
     US 5563142         A    19961008      US 1994-198428    19940222
     US 5489593         A    19960206      US 1994-349694    19941202
PRAI US 1989-457483     A    19891228
     US 1990-603838     A2   19901025
     WO 1990-US7390     A    19901224
     US 1992-904247     B3   19920625
     US 1993-57041      B1   19930430
     US 1994-200094     B1   19940222
OS   MARPAT 116:21074
GI
```



I



II

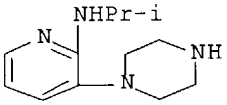
AB Piperazine-containing compds. I [X1, X2, X3 = N or (un)substituted CH, X4 = N, CH, N(O); Z = CH2, CO, COCH2, SO2, CH:CHCO; Rn = H, Me, alkylene, oxo, etc.; R1 = aryl, heteroaryl; R2 = carboxylic ester or amide group, alkyl, etc.] were prepared as anti-AIDS agents (viral reverse transcriptase inhibition data are tabulated). Thus, 2-indolecarboxylic acid was treated with 1-(2-ethoxyphenyl)piperazine in THF in the presence of 1,1'-carbonyldiimidazole to give indolylcarbonylpiperazine II, isolated as the HCl salt.

IT **136818-11-6P 136818-18-3P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
(Reactant or reagent)
(preparation and acylation of, with indolecarboxylic acid)

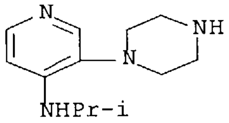
RN 136818-11-6 CAPLUS

CN 2-Pyridinamine, N-(1-methylethyl)-3-(1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 136818-18-3 CAPLUS

CN 4-Pyridinamine, N-(1-methylethyl)-3-(1-piperazinyl)- (9CI) (CA INDEX NAME)

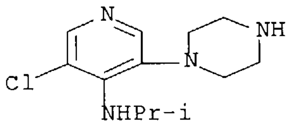


IT **136818-17-2P 136818-78-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)(preparation and catalytic hydrogenation of)

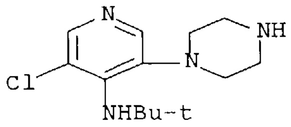
RN 136818-17-2 CAPLUS

CN 4-Pyridinamine, 3-chloro-N-(1-methylethyl)-5-(1-piperazinyl)- (9CI) (CA INDEX NAME)

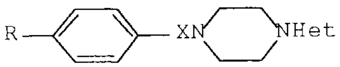


RN 136818-78-5 CAPLUS

CN 4-Pyridinamine, 3-chloro-N-(1,1-dimethylethyl)-5-(1-piperazinyl)- (9CI) (CA INDEX NAME)

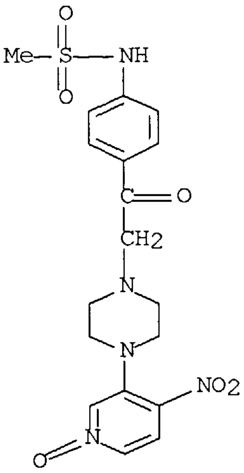


```
L23  ANSWER 36 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1988:94593  CAPLUS Full-text
DN   108:94593
TI   Preparation and formulation of piperazine derivatives as antiarrhythmic
     agents
IN   Cross, Peter Edward; Dickinson, Roger Peter
PA   Pfizer Ltd., UK
SO   Eur. Pat. Appl., 78 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE          APPLICATION NO.   DATE
     ---------------     ----   --------      ---------------   --------
PI   EP 233051            A2    19870819      EP 1987-300978    19870204
     EP 233051            A3    19900321
     EP 233051            B1    19930915
         R:  AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE
     US 4806536           A     19890221      US 1987-10077     19870202
     AT 94534             E     19931015      AT 1987-300978    19870204
     ES 2058105           T3    19941101      ES 1987-300978    19870204
     CA 1303042           A1    19920609      CA 1987-529034    19870205
     FI 8700499           A     19870808      FI 1987-499       19870206
     FI 89265             B     19930531
     FI 89265             C     19930910
     NO 8700483           A     19870810      NO 1987-483       19870206
     AU 8768588           A1    19870813      AU 1987-68588     19870206
     AU 575740            B2    19880804
     JP 62185073          A2    19870813      JP 1987-26203     19870206
     DK 8700608           A     19871005      DK 1987-608       19870206
     DK 165445            B     19921130
     DK 165445            C     19930413
     HU 43584             A2    19871130      HU 1987-478       19870206
     HU 196990            B     19890228
     CN 87100652          A     19870819      CN 1987-100652    19870207
     ZA 8700871           A     19880928      ZA 1987-871       19871206
PRAI GB 1986-3120               19860207
     EP 1987-300978             19870204
GI
```



I

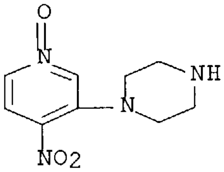
```
AB   Title compds. I [R = R3O2SNH; R3 = C1-4 alkyl, C3-7 cycloalkyl, R1R2N;
     R1, R2 = C1-4 alkyl, R1R2NO2S, O2N, H2N, AcNH; X = (CH2)m (m = 1-4),
     CO(CH2)n, CH(OH)(CH2)n (n = 1-3); Het = (un)substituted 3-, 4-pyridyl or
     2-imidazolyl] and their salts, useful as antiarrhythmics (no data) were
     prepared  1-(4-Pyridyl)piperazine, 4-(MeSO2NH)C6H4COCH2Br, Et3N and EtOH
     were stirred at room temperature for 18 h to give I (R = MeSO2NH; X =
     COCH2; Het = 4-pyridyl).
IT   113049-47-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT
     (Reactant or reagent)
        (preparation and hydrogenation of)
RN   113049-47-1  CAPLUS
CN   Methanesulfonamide, N-[4-[[4-(4-nitro-1-oxido-3-pyridinyl)-1-
     piperazinyl]acetyl]phenyl]- (9CI)  (CA INDEX NAME)
```



IT **113049-46-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)(preparation and reaction of)

RN 113049-46-0 CAPLUS

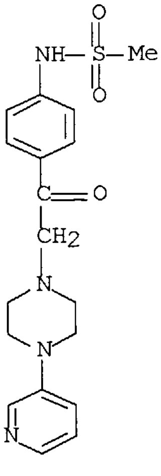
CN Piperazine, 1-(4-nitro-1-oxido-3-pyridinyl)- (9CI) (CA INDEX NAME)



IT **113049-32-4P 113049-33-5P 113049-48-2P 113049-49-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)(preparation of, as antiarrhythmic agent)

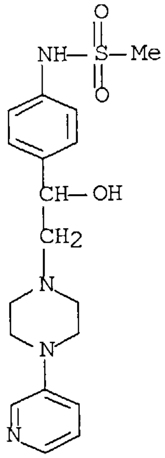
RN 113049-32-4 CAPLUS

CN Methanesulfonamide, N-[4-[[4-(3-pyridinyl)-1-piperazinyl]acetyl]phenyl]- (9CI) (CA INDEX NAME)



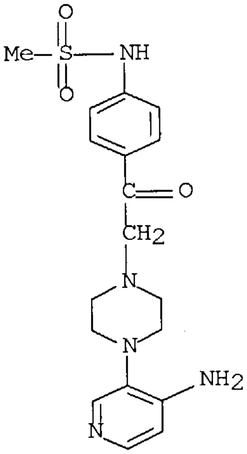
RN 113049-33-5 CAPLUS

CN Methanesulfonamide, N-[4-[1-hydroxy-2-[4-(3-pyridinyl)-1-piperazinyl]ethyl]phenyl]- (9CI) (CA INDEX NAME)



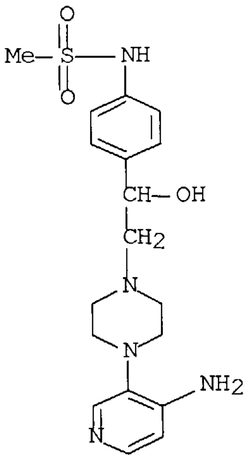
RN 113049-48-2 CAPLUS

CN Methanesulfonamide, N-[4-[[4-(4-amino-3-pyridinyl)-1-piperazinyl]acetyl]phenyl]- (9CI) (CA INDEX NAME)



RN 113049-49-3 CAPLUS

CN Methanesulfonamide, N-[4-[2-[4-(4-amino-3-pyridinyl)-1-piperazinyl]-1-hydroxyethyl]phenyl]- (9CI) (CA INDEX NAME)

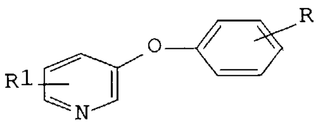


O
Me
S
NH
O
CH
OH
CH2
N
N
NH2
N

L23 ANSWER 37 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1980:181016 CAPLUS Full-text
DN 92:181016
TI 3-Aryloxyaminopyridines
IN Butler, D. E.
PA Warner-Lambert Co., USA
SO Belg., 33 pp.
CODEN: BEXXAL
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 876389	A1	19790917	BE 1979-195269	19790518
	US 4179563	A	19791218	US 1978-907422	19780519
	FR 2426051	A1	19791214	FR 1979-12592	19790517
	FR 2426051	B1	19810306		
	CA 1109468	A1	19810922	CA 1979-327810	19790517
	DE 2920250	A1	19791122	DE 1979-2920250	19790518
	DE 2920250	C2	19880526		
	JP 55000384	A2	19800105	JP 1979-61381	19790518
	GB 2021113	A	19791128	GB 1979-17597	19790521
	GB 2021113	B2	19820707		
PRAI	US 1978-907422		19780519		

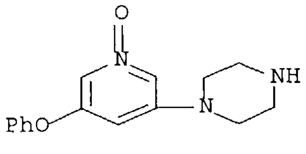
GI



I

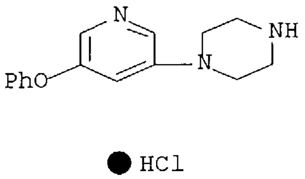
AB (Aryloxy)aminopyridines I [R = H, F, Cl; R1 = 1-piperazinyl, 3-methyl-1-piperazinyl, hexahydro-2-methyl-1H-1,4-diazepin-1-yl, anilino, 2-(dialkylamino)ethylamino], capable of reversal of convulsive electroshock-induced amnesia, were prepared Thus, piperazine and 4-chloro-3-phenoxypyridine in EtOH heated 72 h with stirring gave 3-phenoxy-4-piperazinylpyridine.

IT **73407-25-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)
RN 73407-25-7 CAPLUS
CN Piperazine, 1-(1-oxido-5-phenoxy-3-pyridinyl)- (9CI) (CA INDEX NAME)



IT **73407-26-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and reversal of convulsive electroshock-induced amnesia)
RN 73407-26-8 CAPLUS
CN Piperazine, 1-(5-phenoxy-3-pyridinyl)-, monohydrochloride (9CI) (CA

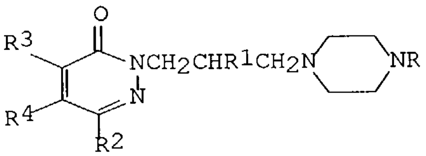
INDEX
NAME)

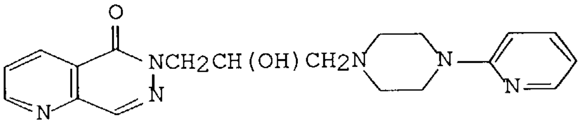


L23 ANSWER 38 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1978:580049 CAPLUS Full-text
DN 89:180049
TI Pyridopyridazinones
IN Heider, Joachim; Kutter, Eberhard; Eberlein, Wolfgang; Austel, Volkhard; Kadatz, Rudolf; Daemmgen, Juergen
PA Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.
SO Ger. Offen., 46 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2708187	A1	19780831	DE 1977-2708187	19770225
PRAI	DE 1977-2708187		19770225		

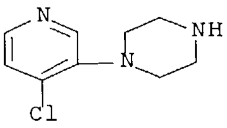
GI


I


II

AB Pyridopyridazinones I [R = pyridyl, halopyridyl, (halo)phenyl, NO2, CF3, C1-3 alkyl, alkoxy; R1 = H, OH; R2 = H, halo, C2-5 alkoxycarbonyl; R3R4 = atoms required to complete pyridine ring] were prepared Thus, treating pyrido[2,3-d]pyridazin-5(6H)-one with epibromohydrin and 1-(2-pyridyl)piperazine gave II. At 1 mg/kg i.v. in dogs II decreased the arterial blood pressure by 45-32 mm Hg, decreased the heart frequency by 7 beats/min., and decreased the femoral blood flow 47%.

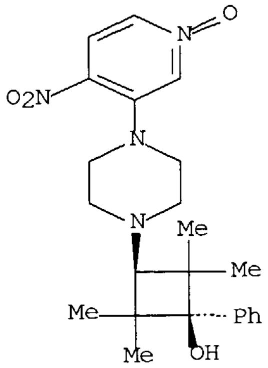
IT **67980-90-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with epoxypropylpyridopyridazinone)
RN 67980-90-9 CAPLUS
CN Piperazine, 1-(4-chloro-3-pyridinyl)- (9CI) (CA INDEX NAME)



```
L23  ANSWER 39 OF 40  CAPLUS  COPYRIGHT 2004 ACS on STN
AN   1975:593390  CAPLUS Full-text
DN   83:193390
TI   Cyclobutane derivatives
IN   Kleemann, Manfred; Kaehling, Joachim; Griss, Gerhart; Hurnaus, Rudolf
PA   Thomae, Dr. Karl, G.m.b.H., Fed. Rep. Ger.
SO   Ger. Offen., 36 pp. Addn. to Ger. Offen. 2,255,439.
     CODEN: GWXXBX
DT   Patent
LA   German
FAN.CNT 2
     PATENT NO.         KIND  DATE          APPLICATION NO.   DATE
     ---------------    ----  --------      ---------------   --------
PI   DE 2349639          A1   19750424      DE 1973-2349639   19731003
     NL 7314672          A    19740514      NL 1973-14672     19731025
     ES 420184           A1   19760316      ES 1973-420184    19731102
     US 3931185          A    19760106      US 1973-413233    19731106
     SU 524516           D    19760805      SU 1973-1967687   19731106
     CH 587253           A    19770429      CH 1973-15633     19731107
     CH 593269           A    19771130      CH 1976-14710     19731107
     CH 602669           A    19780731      CH 1976-14709     19731107
     BE 807162           A1   19740509      BE 1973-137617    19731109
     FR 2206094          A1   19740607      FR 1973-39898     19731109
     ZA 7308606          A    19741127      ZA 1973-8606      19731109
     DD 110271           C    19741212      DD 1973-174561    19731109
     JP 49133383         A2   19741221      JP 1973-126150    19731109
     AU 7362357          A1   19750515      AU 1973-62357     19731109
     HU 167390           P    19750927      HU 1973-TO941     19731109
     GB 1410303          A    19751015      GB 1973-52192     19731109
     AT 7309433          A    19760615      AT 1973-9433      19731109
     AT 334903           B    19770210
     CA 999297           A1   19761102      CA 1973-185407    19731109
     PL 91170            P    19770228      PL 1973-166457    19731110
     PL 92386            P    19770430      PL 1973-182639    19731110
     PL 92387            P    19770430      PL 1973-182640    19731110
     RO 64593            P    19800615      RO 1973-76608     19731110
     ES 427559           A1   19760801      ES 1974-427559    19740622
     SU 528033           D    19760905      SU 1974-2069585   19741023
     SU 561513           D    19770605      SU 1974-2069584   19741023
     AT 7504570          A    19760615      AT 1975-4570      19750616
     AT 334904           B    19770210
     AT 7504571          A    19760615      AT 1975-4571      19750616
     AT 334905           B    19770210
     US 3992536          A    19761116      US 1975-641337    19751216
PRAI DE 1972-2255349          19721111
     DE 1972-2255439          19721111
     DE 1973-2349639          19731003
     US 1973-413233           19731106
     CH 1973-15633            19731107
     AT 1973-9433             19731109
GI   For diagram(s), see printed CA Issue.
AB   Thirty-five piperazinylcyclobutanones (I, R = 2-pyridyl, Ph, p-O2NC6H4,
     o-O2NC6H4, R1 = 4-C2-5 alkyl, 4-cyclohexyl, 2-, 3-, 4-OH, 2-, 3-, 4-Cl,
     2-, 3-Me, H, 4-Ph), useful as sedatives, muscle relaxants, central
     nervous system depressants, and anxiety inhibitors, were obtained in 12-
     74% yields by treatment of II with a substituted bromobenzene in a
     Grignard reaction.
```

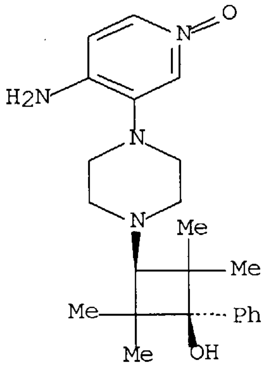
IT **57263-32-8 57263-35-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenation of)
RN 57263-32-8 CAPLUS
CN Cyclobutanol, 2,2,4,4-tetramethyl-3-[4-(4-nitro-1-oxido-3-pyridinyl)-1-piperazinyl]-1-phenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



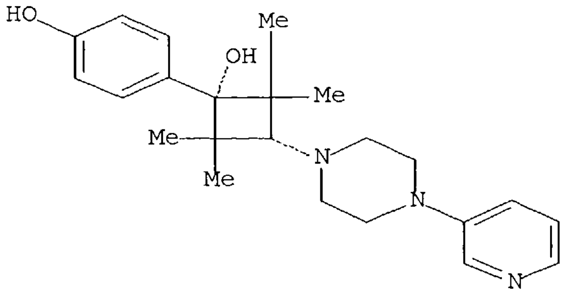
RN 57263-35-1 CAPLUS
CN Cyclobutanol, 3-[4-(4-amino-1-oxido-3-pyridinyl)-1-piperazinyl]-2,2,4,4-tetramethyl-1-phenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



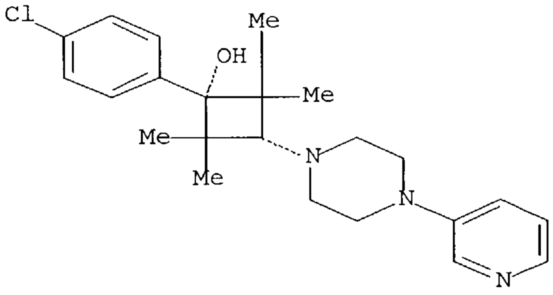
IT **57263-29-3P 57263-30-6P 57263-31-7P**
57263-34-0P 57263-36-2P 57263-37-3P
57263-40-8P 57263-41-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 57263-29-3 CAPLUS
CN Phenol, 4-[1-hydroxy-2,2,4,4-tetramethyl-3-[4-(3-pyridinyl)-1-piperazinyl]cyclobutyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



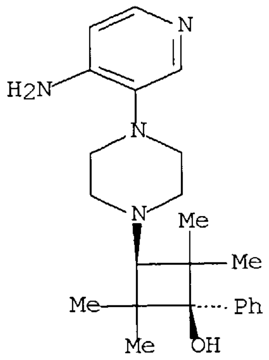
RN 57263-30-6 CAPLUS
CN Cyclobutanol, 1-(4-chlorophenyl)-2,2,4,4-tetramethyl-3-[4-(3-pyridinyl)-
1-
piperazinyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



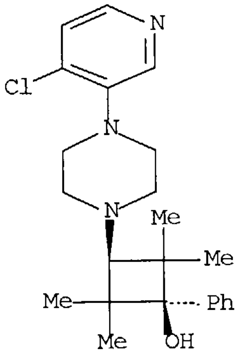
RN 57263-31-7 CAPLUS
CN Cyclobutanol, 3-[4-(4-amino-3-pyridinyl)-1-piperazinyl]-2,2,4,4-
tetramethyl-1-phenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



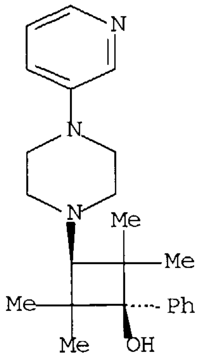
RN 57263-34-0 CAPLUS
CN Cyclobutanol, 3-[4-(4-chloro-3-pyridinyl)-1-piperazinyl]-2,2,4,4-tetramethyl-1-phenyl-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



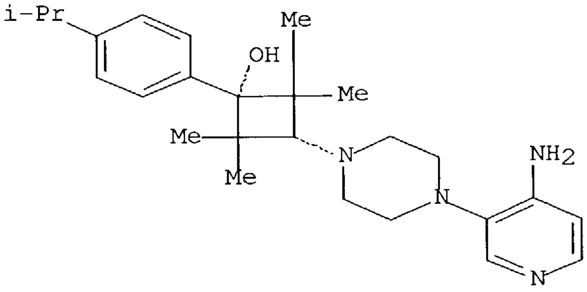
RN 57263-36-2 CAPLUS
CN Cyclobutanol, 2,2,4,4-tetramethyl-1-phenyl-3-[4-(3-pyridinyl)-1-piperazinyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



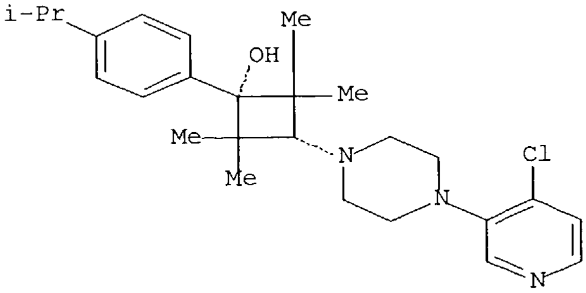
RN 57263-37-3 CAPLUS
CN Cyclobutanol, 3-[4-(4-amino-3-pyridinyl)-1-piperazinyl]-2,2,4,4-tetramethyl-1-[4-(1-methylethyl)phenyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



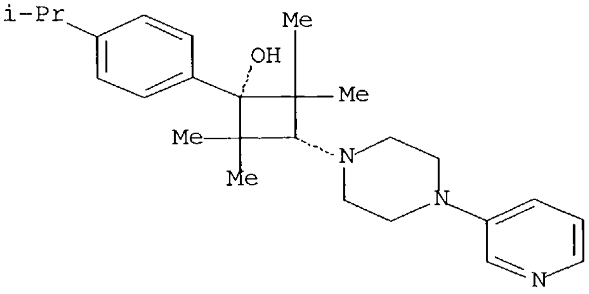
RN 57263-40-8 CAPLUS
CN Cyclobutanol, 3-[4-(4-chloro-3-pyridinyl)-1-piperazinyl]-2,2,4,4-tetramethyl-1-[4-(1-methylethyl)phenyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



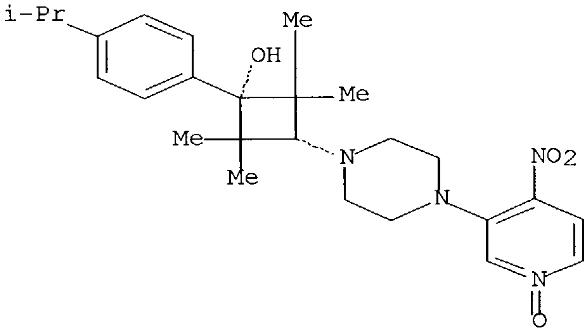
RN 57263-41-9 CAPLUS
CN Cyclobutanol, 2,2,4,4-tetramethyl-1-[4-(1-methylethyl)phenyl]-3-[4-(3-pyridinyl)-1-piperazinyl]-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



IT **57263-38-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with 3-bromo-4-nitropyridine 1-oxide)
RN 57263-38-4 CAPLUS
CN Cyclobutanol, 2,2,4,4-tetramethyl-1-[4-(1-methylethyl)phenyl]-3-[4-(4-nitro-1-oxido-3-pyridinyl)-1-piperazinyl]-, cis- (9CI) (CA INDEX NAME)

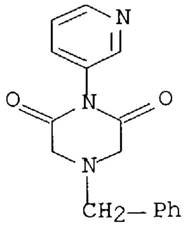
Relative stereochemistry.



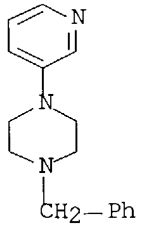
L23 ANSWER 40 OF 40 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1967:37889 CAPLUS Full-text
DN 66:37889
TI A facile synthesis of piperazines from primary amines
AU Henry, David W.
CS Stanford Res. Inst., Menlo Park, CA, USA
SO Journal of Heterocyclic Chemistry (1966), 3(4), 503-11
CODEN: JHTCAD; ISSN: 0022-152X
DT Journal
LA English
OS CASREACT 66:37889
GI For diagram(s), see printed CA Issue.

AB A general procedure is described for converting primary amines to N-substituted piperazines. Reaction of an amine with an N-substituted iminodiacetic acid anhydride yields an iminodiacetic acid monoamide, which closes to a 2,6-piperazinedione (I) upon treatment with Ac_2O. The diones are reduced to piperazines with borane-tetrahydrofuran. Fourteen examples of this process, using twelve aliphatic or aromatic amines and three iminodiacetic acids, are presented. Yields of piperazines, based upon starting amine, ranged from 21 to 52%. The procedure is rapid and no purification problems were encountered. Alternate methods for preparing the 2,6-piperazinedione intermediates are discussed.

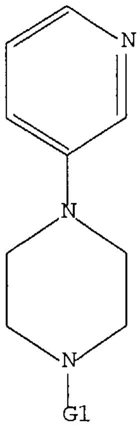
IT **13480-17-6P 13480-30-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 13480-17-6 CAPLUS
CN 2,6-Piperazinedione, 4-benzyl-1-(3-pyridyl)- (8CI) (CA INDEX NAME)



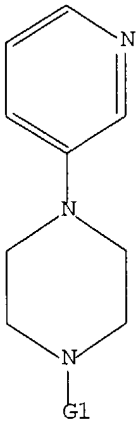
RN 13480-30-3 CAPLUS
CN Piperazine, 1-(phenylmethyl)-4-(3-pyridinyl)- (9CI) (CA INDEX NAME)



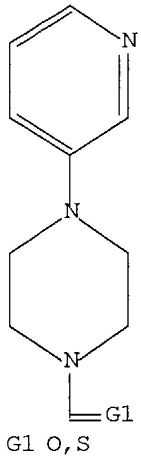
```
=> d l1; d l4; d l7; d l11l d l15; d l19; d his; log y
L1 HAS NO ANSWERS
L1                STR
```



```
 G1 H,Cb,Ak

Structure attributes must be viewed using STN Express query preparation.

L4 HAS NO ANSWERS
L4                STR
```



```
 G1 H,Cb,Ak


Structure attributes must be viewed using STN Express query preparation.



L7 HAS NO ANSWERS
L7                STR
```



```
Structure attributes must be viewed using STN Express query preparation.


L19 HAS NO ANSWERS
L19                STR

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY -  AVAILABLE VIA OFFLINE PRINT *

Structure attributes must be viewed using STN Express query preparation.

     (FILE 'HOME' ENTERED AT 12:45:53 ON 15 JUL 2004)

     FILE 'REGISTRY' ENTERED AT 12:46:00 ON 15 JUL 2004
L1                 STRUCTURE UPLOADED
L2             32 S L1
L3            636 S L1 FUL
L4                 STRUCTURE UPLOADED
L5             24 S L4 SAM SUB=L3
L6            487 S L4 FUL SUB=L3
L7                 STRUCTURE UPLOADED
L8              8 S L7 SAM SUB=L6
L9            126 S L7 FUL SUB=L6
L10           361 S L6 NOT L9
L11                STRUCTURE UPLOADED
L12             9 S L11 SAM SUB=L10
L13           186 S L11 FUL SUB=L10
L14           175 S L10 NOT L13
L15                STRUCTURE UPLOADED
L16             5 S L15 FUL SUB=L14
L17           170 S L14 NOT L16

     FILE 'CAPLUS' ENTERED AT 12:53:43 ON 15 JUL 2004
L18            46 S L17

     FILE 'REGISTRY' ENTERED AT 12:53:53 ON 15 JUL 2004
L19                STRUCTURE UPLOADED
L20            24 S L19 FUL SUB=L17
L21           170 S L17 NOT L0
L22           146 S L17 NOT L20
```

```
     FILE 'CAPLUS' ENTERED AT 12:56:54 ON 15 JUL 2004
L23          40 S L22

COST IN U.S. DOLLARS                             SINCE FILE     TOTAL
                                                      ENTRY   SESSION
FULL ESTIMATED COST                                  201.30    552.21

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)       SINCE FILE     TOTAL
                                                      ENTRY   SESSION
CA SUBSCRIBER PRICE                                  -29.40    -29.40

STN INTERNATIONAL LOGOFF AT 12:58:24 ON 15 JUL 2004
```